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ELECTROENCEPHALOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF SUPRATENTORIAL TUMORS

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SEVERAL studies have been reported showing a general correlation between the malignancy and rapidity of tumor growth in the brain and the severity of the electroencephalographic changes recorded before operation. The most noteworthy are those of Walter and Dovey [1] and Cobb,[2] in England, and of Yeager and Luse,[3] Greenstein and Strauss [4] and Hoefer and co-workers [5] on this continent.

The present report is an attempt to see whether this correlation can be carried a step further. An attempt has been made to determine what features in the electroencephalogram are of value in predicting the type of tumor that is present. This study has been limited to verified supratentorial tumors.

MATERIAL AND METHODS

Analysis was made of 100 consecutive cases of patients with supratentorial tumors who had an adequate electroencephalographic examination and were operated on. The clinical, laboratory and roentgenographic data, the surgeon's findings at operation and the pathologic specimens and autopsy material were all correlated with the records.

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Read at the Second Annual Meeting of the American Electroencephalographic Society, Atlantic City, N. J., June 12, 1948.

1. Walter, W. G., and Dovey, V. J.: Encephalography in Cases of Subcortical Tumor, J. Neurol., Neurosurg. & Psychiat. **7**:57-65, 1944.

2. Cobb, W. A.: The Electroencephalographic Localization of Intracranial Neoplasms, J. Neurol., Neurosurg. & Psychiat. **7**:96-102, 1944.

3. Yeager, C. L., and Luse, S.: Electroencephalographic Localization and Differentiation of Lesions of the Frontal Lobes, Arch. Neurol. & Psychiat. **54**:197-204 (Sept.) 1945.

4. Greenstein, L., and Strauss, H. J.: Correlation Between the Electroencephalogram and the Histological Structure of Gliogenous and Metastatic Brain Tumors, J. Mt. Sinai Hosp. **12**:874-877, 1945.

5. Hoefer, P. F. A.; Schlesinger, E. B., and Pennes, H. H.: Clinical and Electroencephalographic Findings in a Large Series of Verified Brain Tumors, Tr. Am. Neurol. A. **71**:52-57, 1945.

The group consisted of (table 1) 25 patients with glioblastoma multiforme, 21 with astrocytoma, 28 with meningeal tumors and 26 with miscellaneous tumors, including metastic lesions, the less frequent gliomas and tumors of the pituitary region.

The method of examination was essentially the same as that previously described in use at the Montreal Neurological Institute[6]; extra electrode placements and a nasal electrode were used frequently when necessary for localization studies.

ACCURACY OF ELECTROENCEPHALOGRAPHIC LOCALIZATION

If the surgeon had done a craniotomy over the site of the electroencephalographic localization and at least about one third of the tumor was present, the electroencephalogram was accepted as correct. Other-

TABLE 1.—*Classification of One Hundred Supratentorial Tumors*

Types		No. of Cases
Glioblastoma multiforme		25
Astrocytoma		21
Astrocytoma diffusum	10	
Gemistocytic astrocytoma	4	
Fibrillary astrocytoma	3	
Astrocytoma, type not determined	4	
Meningeal tumors		28
Meningeal fibroblastoma	25	
Parasagittal tumors	12	
Tumors of the sphenoidal ridge	7	
Meningeal sarcoma	3	
Miscellaneous tumors		26
Carcinoma, metastatic	5	
Glioma, unclassified	5	
Oligodendroglioma	3	
Astroblastoma	2	
Oligodendroblastoma	1	
Ganglioneuroma	1	
Hemangioendothelioma	2	
Perithelial sarcoma	1	
Lymphosarcoma	1	
Pinealoma	1	
Craniopharyngioma	2	
Pituitary adenoma	2	

wise, it was regarded as poor. On this basis, 77 per cent of the lesions were correctly localized, 20 per cent were poorly localized and 3 per cent were on the wrong side (table 2).

Glioblastomas were best localized, with 92 per cent correct; meningeal tumors were correctly localized in 82 per cent of cases and astrocytomas in 76 per cent. The percentage of correct localizations was the same in various parts of the cerebral hemispheres, but tumors of the third ventricle were very poorly localized, only 29 per cent, or 2 out of 7, being accurately localized. It is hoped that at least one outcome of the present study will be an improvement in this figure.

6. Jasper, H. H.; Kershman, J., and Elvidge, A. R.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44**:328-348 (Aug.) 1940.

Localization on the Wrong Side.—In 3 cases (1 each of glioblastoma, astrocytoma and meningeal tumor) localization was on the wrong side, and it is important to understand why this happened. In each case,

TABLE 2.—*Accuracy of Electroencephalographic Localization*

	Number of Cases	Correct, Percentage	Poor, Percentage	Wrong Side, Percentage
Total	100	77	20	3
Glioblastoma	25	92	4	4
Astrocytoma	21	76	19	5
Meningeal tumor	28	82	14	4
Frontal region	35	83	14	3
Temporal region	31	81	16	3
Parieto-occipital region	20	85	15	0
Third ventricle	7	29	71	0

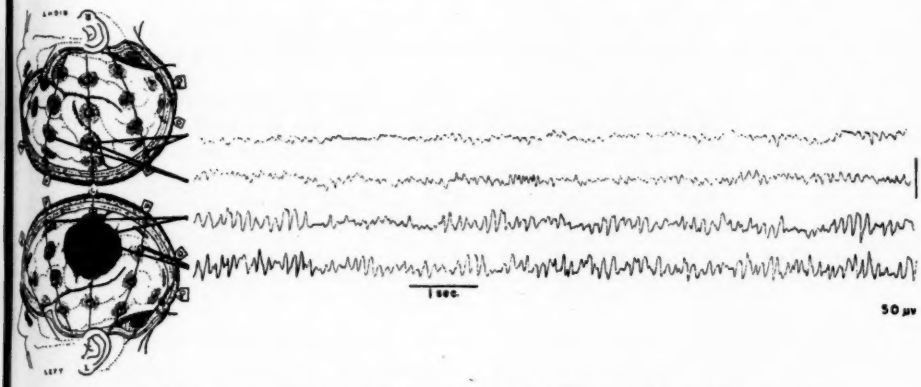

Fig. 1 (case 1).—Glioblastoma in the left frontal and anterior parietal region. The extent of the tumor is outlined in the dark shaded area in the lower head chart. The upper two tracings are from the right side and indicate a relatively quiet area on the normal side as compared to the side of the tumor, shown in the lower two tracings.

the electroencephalographic localization was based on the presence of a quiet area in the homologous region of the hemisphere, opposite to the site of the actual tumor. In each case, over the site of the tumor there were potentials which had frequencies between 8 and 10 per second —i. e., in the range of normal alpha activity—but the amplitude was higher than in the normal side. This led to the diagnosis of a neoplasm as indicated by a quiet area on the wrong side. These cases represent a failure to recognize that pathologic discharges may sometimes have the same frequency as alpha waves, though they usually have a higher voltage. The following case illustrates this error.

CASE 1.—*Quiet area on the side opposite the tumor.*

J. P., a 58 year old man, had a clinical history of only five weeks' duration consisting of bifrontal headache, difficulty in speech and focal seizures which began in the right side of the body. Neurologic examination revealed a mild papilledema, clumsiness in the right hand and incoordination of the right leg. Roentgenograms and a pneumoencephalogram indicated the presence of a large expanding intracranial lesion involving the posterior part of the left frontal and anterior left parietal regions. This was confirmed at operation, when a glioblastoma was found with a small cyst at a depth of 1½ inches (3 cm.) from the surface of the cortex.

In the preoperative electroencephalogram, the only abnormality was an asymmetry with a relatively quiet area in the right central region, as shown in figure 1.

INCIDENCE AND RELATIVE IMPORTANCE OF VARIOUS FORMS OF FOCAL ELECTROENCEPHALOGRAPHIC ABNORMALITY

Table 3 shows how often various kinds of focal abnormality were found in the 100 patients, with an analysis of the occurrence of each of these abnormalities in the different types of tumors.

TALLE 3.—*Per Cent Incidence of Focal Electroencephalographic Abnormalities in Patients with Various Types of Tumors*

	Number of Cases	Focal <1, %	Focal 1-2, %	Focal 2-3, %	Focal 4-7, %	Focal Sharp, %	Focal Spike, %	F. <12 Rhythm, %	Superficial Phase Reversals, %	Quiet Area, %
Total	100	57	69	41	75	59	21	31	47	6
Glioblastoma	25	72	92	52	84	52	20	52	40	4
Astrocytoma	21	29	48	24	76	86	33	33	66	10
Meningeal T.	28	60	70	36	71	61	25	22	44	11
Miscellaneous	26	65	65	50	69	42	8	19	38	0

It can be seen that focal 4 to 7 per second waves occurred in 75 per cent of all patients with tumors and occurred in almost the same high proportion in each of the various types of tumors. This was therefore the most commonly occurring electroencephalographic abnormality and by itself was of no value in the differential diagnosis of the various tumor types

Focal slow waves at 3 per second and less were seen much oftener in glioblastoma multiforme than in other tumors. Activity in this range was relatively infrequent in astrocytomas but was commoner in meningeal and miscellaneous tumors. Focal 1 to 2 per second waves were particularly significant since they were present in 92 per cent, or nearly all, of the glioblastomas, and focal less than 1 per second waves were almost as constant. Both these frequencies were much less common in astrocytomas but occurred fairly often in meningeal tumors. The significance of these facts will be discussed later.

Focal sharp waves occurred in 86 per cent of all the astrocytomas, and less commonly in meningeal tumors and glioblastomas. Focal spikes were also seen oftener in astrocytomas than in the other two groups.

Superficial phase reversals were more likely to be associated with astrocytoma than with other tumor types, but they were seen in nearly 50 per cent of all tumors.

Focal quiet areas were not very common in the entire group (6 per cent) and were misleading (as previously described) in half the cases in which they occurred.

INCIDENCE AND RELATIVE IMPORTANCE OF OTHER ELECTROENCEPHALOGRAPHIC ABNORMALITIES

Table 4 shows the incidence of other electroencephalographic qualities in the various tumor groups.

TABLE 4.—*Per Cent Incidence of Other Electroencephalographic Abnormalities in Patients with Various Types of Tumors*

	Number, %	Spread to Opposite Side, %	Bilaterally Synchronous Abnormality		Asymmetry, P-0, %	Epilepsy, %	Focal Fast Activity with Epilepsy, %	Focal Fast Activity Without Epilepsy, %
			2-3, %	4-7, %				
Total	100	33	11	18	56	45	30	30
Glioblastoma	25	24	4	12	80	44	24	32
Astrocytoma	21	29	10	24	57	71	61	24
Meningeal T.	28	42	7	18	42	40	18	42
Miscellaneous	26	35	23	19	46	30	23	19

Spread of Focal Abnormality to the Opposite Side.—This was more frequent in meningeal than in other tumors, occurring in 42 per cent. The explanation may lie in the tendency for this tumor to occur in parasagittal and basal regions (table 1).

Bilaterally Synchronous Abnormality.—This may be distinguished from simple spread to the opposite hemisphere by the time element and the fact that bisynchronous waves usually have a rhythmic rather than random pattern. Bisynchrony is not commonly observed in hemispheral tumors but it was a significant feature of tumors in and near the third ventricle. Bilaterally synchronous 4 to 7 per second waves occurred in 86 per cent of the third ventricle tumors and in only 13 per cent of hemispheral tumors, while bisynchronous 2 to 3 per second waves were seen in 43 per cent, or nearly half, of the third ventricle tumors and in only 9 per cent of hemispheral tumors. Bilateral slowing of the parieto-occipital alpha rhythm and generalized sharp activity were also commonly seen in tumors around the third ventricle.

Asymmetry of the Parieto-Occipital Alpha Activity.—Regardless of the location of the tumor, the parieto-occipital alpha activity was asymmetric in 80 per cent of the glioblastomas. This was seen in slightly less than half of the meningeal tumors and slightly more than half of the astrocytomas. In the latter groups it occurred only in tumors affecting the parieto-occipital region.

Relation of Focal Sharp Waves and Spikes to Clinical Seizures.—A history of either major or minor seizures occurred much more frequently in patients with astrocytoma (71 per cent) than in any of the other groups. In nearly all the patients with astrocytoma (61 per cent out of 71 per cent) a history of clinical seizures was associated with the presence of focal sharp or spike activity. On the other hand, the poorest correlation was seen in the meningeal tumors; although 40 per cent of the patients gave a history of epilepsy, this was accom-

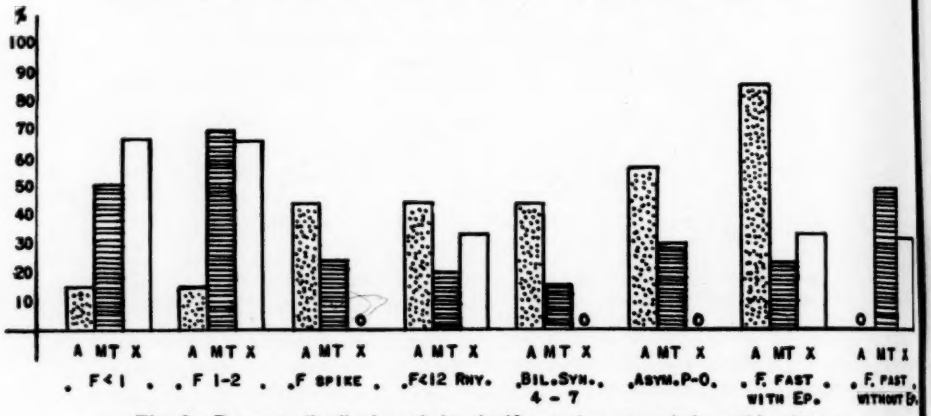

Fig. 2.—Per cent distribution of the significant electroencephalographic abnormalities for tumors of the frontal regions. *A* indicates astrocytoma; *MT*, meningeal tumor; *X*, miscellaneous tumors; *F*, focal; *P-O*, parieto-occipital region; *Ep*, epilepsy. Further description is contained in the text.

panied with focal fast waves in only 18 per cent, and there were 42 per cent who had focal sharp activity in the electroencephalogram without a history of clinical seizures. This lack of correlation when contrasted with the astrocytomas is of differentiating significance.

ELECTROENCEPHALOGRAPHIC ABNORMALITY AND LOCATION

If the localization of the electroencephalographic abnormality is taken into account, some further refinement is possible in the prognosis of the type of tumor.

Frontal Region.—Of the 35 tumors in this region, 20 were meningeal, 7 were astrocytomas and only 2 were glioblastomas, while 6 belonged to the miscellaneous group.

The main features differentiating the two commonest types of neoplasm in this region—namely, meningeal tumor and astrocytoma—have been charted from a statistical analysis and illustrated in figure 2. They may be summarized as follows:

A meningeal tumor is suggested by the presence of focal less than 1 and 1 to 2 per second waves and by the occurrence of focal sharp waves without a clinical history of seizures.

An astrocytoma is suggested by the presence of focal spikes, a history of epilepsy associated with the occurrence of focal sharp waves and spike discharges and by the absence of focal less than 1 and 1 to 2 per second activity, the presence of focal rhythmic activity and asymmetry in the parieto-occipital regions. It is of interest to note in figure 2 that in the miscellaneous group of tumors, there were none

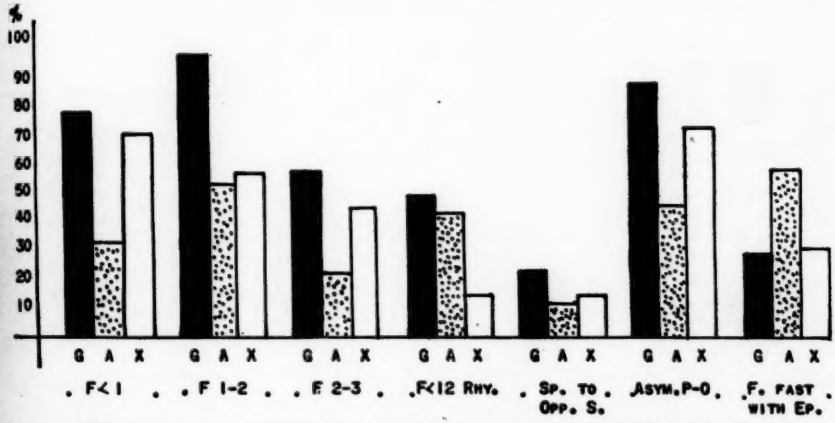

Fig. 3.—Per cent distribution of the significant electroencephalographic abnormalities for tumors of the temporal region and vicinity. *G* indicates glioblastoma multiforme; *A*, astrocytoma; *X*, miscellaneous tumors; *F*, focal. Further description is contained in the text.

with focal spikes and none had any asymmetry of the parieto-occipital alpha.

Temporal Region and Vicinity.—Of the 31 tumors in this location, 14 were glioblastomas, 9 were astrocytomas and only 1 was meningeal. There were 7 miscellaneous tumors. The main differentiating features have been compared in figure 3 and may be summarized as follows:

Glioblastoma is suggested by the presence of focal slow waves at less than 1 to 3 per second, by spread of abnormality to the opposite side and by asymmetry in the parieto-occipital regions.

Astrocytoma is indicated by the relative absence of these findings and the presence of focal fast activity associated with clinical seizures.

Parietal and Occipital Regions.—There were 20 tumors in this region, and the various tumor types were more evently distributed. There were 5 glioblastomas, 4 astrocytomas, 7 meningeal tumors and 4 miscellaneous types. Since each group was small, apparent statistical differences might not be very significant.

The diagnostic electroencephalographic features of the tumor types in this region were similar to those for the hemispheres generally, and will be summarized subsequently.

These differentiating factors in the electroencephalogram can best be illustrated by the following three patients, each of whom had a different neoplasm involving approximately similar parts of the brain.

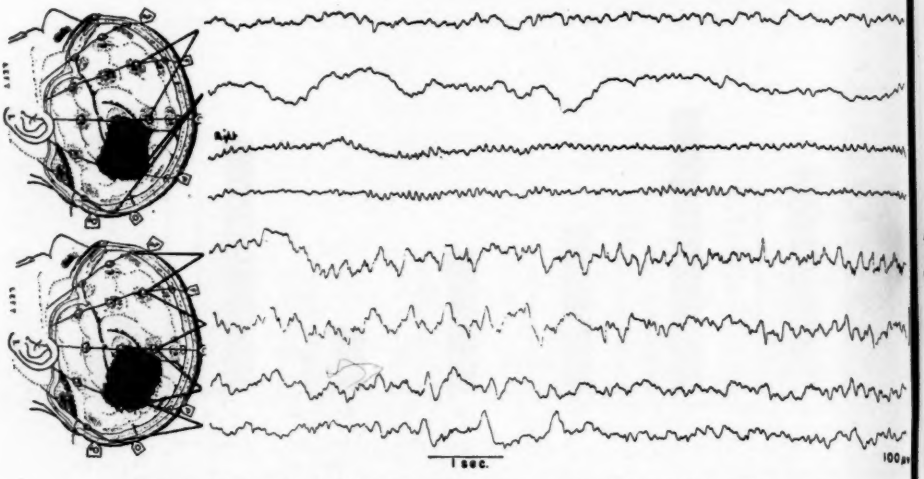

Fig. 4 (case 2).—Glioblastoma multiforme in the left parietal region. The upper two lines are from the left side as indicated; the second set of two lines, from the right homologous regions. There is a continual discharge of variable high voltage slow activity and less than 1 to 3 per second with 4 to 7 per second and sharp waves in the lower four lines. There is no spread of abnormality to the opposite side and few superficial phase reversals.

CASE 2.—*Glioblastoma multiforme in the left parietal region.*

F. P. C. had a glioblastoma multiforme located chiefly in the left parietal region and spreading into the temporal region. He was a 55 year old man with a history of focal seizures for four months, difficulty in reading for three months, changes in personality, inability to concentrate and nominal aphasia for three days before admission. On examination, he showed early papilledema, a right homonymous hemianopsia, coarse tremor and weakness of the right hand with some sensory changes on the right side and nominal aphasia.

The electroencephalogram (fig. 4) showed a continual discharge of variable high voltage slow activity at less than 1 to 3 per second, with 4 to 7 per second and sharp waves. There was practically no spread of the abnormality to the opposite side and few if any superficial phase reversals even when recording was done across the site of the neoplasm.

CASE 3.—*Right parietal parasagittal meningeal fibroblastoma.*

E. B., a 42 year old man with a right parietal parasagittal meningeal fibroblastoma had complained of headache for two years and gradually failing vision in the right eye. There had been blindness of the left eye due to an opacity of the lens for eight years and occasional morning dizziness for six years. There was no history of seizures. On examination, there was papilledema of 1 D. in the right optic disk; the left pupil was larger than the right, and there was nystagmus on gaze to the right.

His electroencephalogram (fig. 5) showed a moderate amount of slow activity at mixed frequencies but mainly varying from 3 to 7 per second without much less activity than 1 or 1 to 2 per second. There was a considerable amount of bilateral spread (even though there was only a very small neoplasm on the opposite side) and there was a considerable amount of sharp wave discharges despite the absence of clinical seizures.

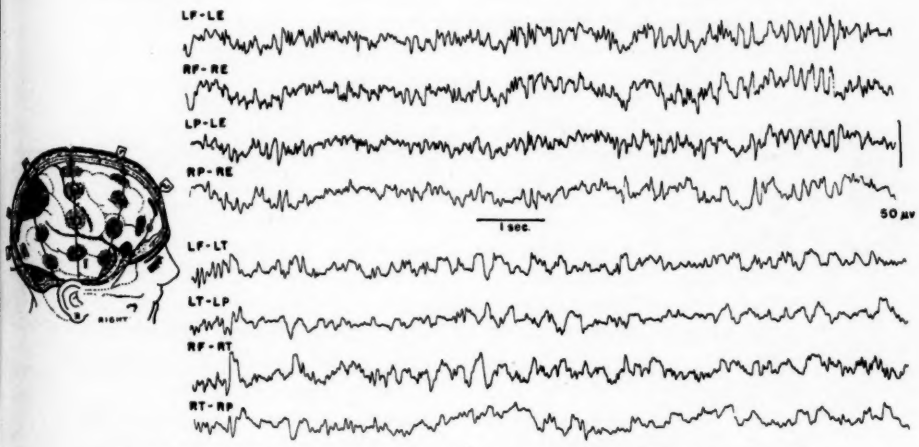

Fig. 5. (case 3).—Right parietal parasagittal meningeal fibroblastoma. *LF* indicates left frontal; *RF*, right frontal; *LP*, left parietal; *RP*, right parietal; *LE*, left ear, *RE*, right ear; *LT*, left temporal; *RT*, right temporal. There is a moderate amount of slow activity, varying from 3 to 7 per second with very little less than 1 to 2 per second. There are a great deal of bilateral spread and a considerable amount of sharp wave discharges despite the absence of clinical seizures.

CASE 4.—*Astrocytoma in the right parietal region.*

J. P. had an astrocytoma diffusum involving the right parietal region. He was 39 years old and gave a history of headache for about ten years, slight weakness of the left leg for about two years and convulsions which began with flashing lights about two weeks before admission. On examination, he had a moderate bilateral papilledema and loss of two point discrimination and joint sensibility on the left side.

His electroencephalogram (fig. 6) showed occasional random waves at 2 to 3 per second, no spread of the abnormality to the opposite side, focal sharp waves (with a history of clinical seizures) and superficial phase reversals over the site of the neoplasm.

The results of this survey are summarized in table 5. It is obvious that no single characteristic is pathognomonic of any of the three main types of tumor. The diagnosis of each type is suggested by the simultaneous presence of a constellation of certain electroencephalographic findings and the relative absence of others. Thus, a glioblastoma should be suspected if there is a considerable amount of focal less than 1 to 2 per second and 2 to 3 per second activity and focal rhythmic activity at less than 12 per second with few or no focal fast discharges and few superficial phase reversals.

A meningeal tumor is most likely to be present if there is a moderate amount of focal less than 1 to 3 per second activity, spread of the abnormality to the opposite side and focal sharp activity despite the absence of a clinical history of epilepsy, or the presence of the latter without focal sharp or spike discharges.

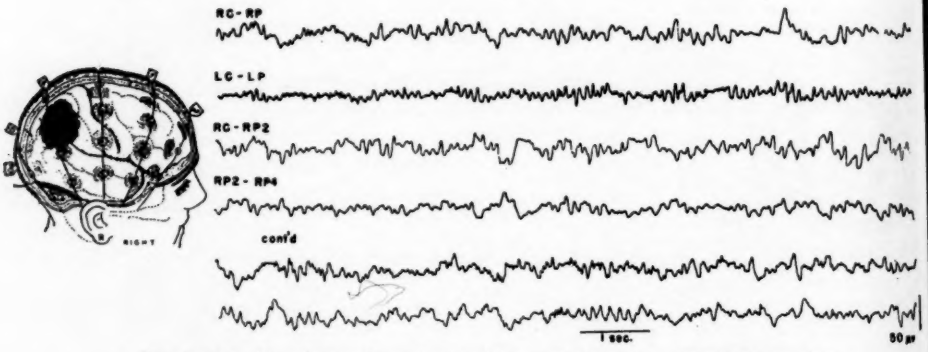

Fig. 6 (case 4).—Astrocytoma in the right parietal region. *RC* indicates right central; *RP*, right parietal, *LC* and *LP*, left central and left parietal; *RP2*, a medial right parietal and *RP4*, a more lateral right parietal placement as shown on the head chart. There are occasional random waves as 2 to 3 per second, no abnormality on the opposite side, focal sharp waves (with a history of seizures) and superficial phase reversals over the site of the neoplasm.

TABLE 5.—*Electroencephalographic Criteria in Differential Diagnosis of Chief Types of Tumor*

	Glioblastoma	Meningeal Tumor	Astrocytoma
Occurrence	+++	+++	+++
Focal <1-2/sec.	++++	++	+
Focal 2-3/sec.	++++	++	+
Focal <12/sec. rhythms	++++	++	+
Focal fast without epilepsy	++	+++	+
Spread to opposite side	++	++++	++
Superficial phase reversals	++	+	++++
Focal sharp	+	+	++++
Focal fast with epilepsy	+	+	++++

An astrocytoma is indicated if focal less than 1 to 3 per second activity is absent or infrequent, there is a considerable amount of focal sharp and spike activity accompanying a history of clinical epilepsy and there are many superficial phase reversals.

COMMENT

Brain tumors are themselves electrically inactive.[7] The changes they produce in the electroencephalogram must be the result of their effect on the adjacent brain and depend on their location, size and other factors.

In the present study an attempt was made to see whether different tumor types produced characteristic electroencephalographic alterations. Attention was focused on the three commonest neoplasms, glioblastoma multiforme, astrocytoma and meningeal tumors, and the wave patterns were carefully analyzed and correlated with the clinical and other findings, to see whether the electroencephalogram could be used to make a preoperative pathologic diagnosis.

Histopathologically these three kinds of tumors have quite different characteristics and affect the brain differently. Glioblastoma multiforme is very rapidly growing, is pleomorphic and shows peculiar and almost specific vascular alterations. There is a striking endothelial and adventitial proliferation within the tumor and in some instances in the brain near it.[8] With this is a considerable amount of degeneration and necrosis. In contrast, astrocytoma shows little vascular change, is very much slower growing, arises in the white matter and produces relatively mild changes in cortical cells, usually late in its growth.

This contrast is reflected in the electroencephalogram by the sharp difference in the amount of focal less than 1 to 3 per second activity occurring in the two tumors. Slow waves in this range, and especially at 1 to 2 per second, were seen in nearly all glioblastomas but were much less common in astrocytomas. Previous studies (e. g., in head injury, etc.) have shown that the amount of slowing of the frequency patterns was, in general, an index of the amount of injury to cortical cells. The greater amount of less than 1 to 3 per second reflects the greater severity of damage to the nerve cells caused by glioblastoma both directly through local pressure and indirectly through vascular alterations.

Meningeal tumors also exhibit a considerable amount of less than 1 to 2 per second activity. This is probably the result not only of direct pressure on the cortex but of the interference with the venous

7. Foerster, O., and Altenburger, H.: Elektrobiologische Vorgänge an der menschlichen Hirnrinde, Deutsche Ztschr. f. Nervenh. **135**:277-288, 1935.

8. Penfield, W. G.: The Classification of Gliomas and Neuroglia Cell Types, Arch. Neurol. & Psychiat. **26**:745-753 (Oct.) 1931.

circulation from the cortex caused by the tumor. Activity in this range is therefore the result of both physical and metabolic changes in nerve cells.

It was surprising that all three types of tumor showed practically the same high amount of focal 4 to 7 per second activity (table 4). Even among the largely subcortical astrocytomas, 76 per cent had focal 4 to 7 per second waves, and in the extracerebral meningiomas 70 per cent showed these wave forms. They were also present in 69 per cent of the miscellaneous tumors and 84 per cent of the glioblastomas. Because focal 4 to 7 per second waves are so common, they are most likely the result of any kind of disturbance of cortical function either by direct pressure, through vascular changes, or by interference with subcortical neuronal pathways as in astrocytoma.

Walter's hypothesis [9] that 4 to 7 per second waves suggest involvement of deep structures, and especially of corticothalamohypothalamic centers, does not seem tenable in view of the high percentage of extracerebral meningeal tumors in which these frequencies occur and the fact that they are almost as common in meningeal tumors as in subcortical astrocytomas. In the present study it was found that deep tumors such as those involving the third ventricle showed bilaterally synchronous 5 to 6 per second waves. It is felt that this bilateral synchrony, rather than focal 4 to 7 per second waves, was the characteristic of interference with normal corticohypothalamic relations and that there probably was a pacemaker in the walls of the third ventricle capable of discharging rhythmic 5 to 6 per second waves synchronously to both hemispheres and disturbing the cortical alpha rhythm. A similar conclusion has been suggested by Cobb.[2]

The very frequent occurrence of parieto-occipital assymmetry in patients with glioblastoma multiforme (80 per cent) is probably due to the greater predilection for these tumors to invade the temporal regions and involve the optic radiations.

In view of the emphasis previously placed on the close association between the occurrence of focal spikes and focal sharp waves and focal clinical seizures,[10] it is interesting to note that 30 per cent of all the patients in this group had focal fast activity without a history of seizures. The greatest dissociation was in the group with meningeal tumors; 22 per cent had focal spikes, and a total of 42 per cent had spikes or sharp waves or both without a history of clinical seizures

9. Walter, W. G.: Discussion of the Electroencephalogram in Organic Cerebral Disease, Proc. Roy. Soc. Med. **41**:237-250, 1948.

10. Jasper, H. H., and Kershman, J.: Electroencephalographic Classification of the Epilepsies, Arch. Neurol. & Psychiat. **45**:903-943 (June) 1941. Jasper, H. H.: Electroencephalography, in Penfield, W. G., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill. Charles C Thomas, Publisher, 1941, chap. 14.

before operation. The closest correlation between focal fast activity and seizures was in the astrocytoma group, and this is a useful diagnostic point.

These observations reemphasize the lack of knowledge concerning the relation between the presence of pathologic discharges in the electroencephalogram and the occurrence of a clinical seizure. Obviously focal spikes and sharp waves may be present for a considerable time without the appearance of a seizure. Some additional factor is apparently necessary to spark the clinical attack. However, the evidence of these focal spikes and sharp waves in the cortex adjacent to a meningeal tumor, despite the absence of seizures preoperatively, partly explains why in so many instances seizures may begin after the tumor has been removed.[11] It indicates that potentially irritable cortex lies beneath or near the site of the meningioma and the occurrence of seizures does not depend on postoperative scar formation only.

Finally it must be emphasized that the diagnosis of brain tumor cannot be made from the electroencephalogram alone. None of the electroencephalographic alterations are specific for neoplasm, and all the changes which have been described have been seen in a wide variety of other intracranial lesions, such as abscesses, vascular lesions, encephalitis, etc. Indeed, in many instances similar electroencephalographic abnormalities have been observed without any obvious organic lesions (in the so-called "idiopathic" epilepsies, in behavior problems in children, in psychopathic personalities, etc.).

Like most laboratory tests, the electroencephalogram becomes significant only if correlated with the clinical history, physical examination and other findings, such as roentgenograms, spinal fluid studies and others. Table 5, showing the summary of various electroencephalographic characteristics for each of the main tumor types, should be used only with this kind of orientation. So-called "blind analysis" of the electroencephalogram has very little clinical value. The electroencephalogram must be evaluated as part of a constellation of data on the patient, and, by a skillful blending of all the available information, the electroencephalogram can make its greatest contribution toward the clarification of the individual problem presented by each patient.

From this point of view, there are certain broad indications in the electroencephalogram which can help in predicting the type of tumor present.

SUMMARY AND CONCLUSIONS

A detailed analysis is made of the clinical data, roentgenograms, observations at operation, pathologic material and electroencephalograms of 100 patients with supratentorial tumors who had come to operation.

11. Penfield, W. G., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

There are no electroencephalographic characteristics typical of brain tumor. The analysis of the electroencephalogram and its interpretation should be done in conjunction with all the available clinical data.

Although there are no single electroencephalographic abnormalities typical of the various types of tumors, if the record is evaluated in conjunction with other available data the following criteria help to differentiate the commonest supratentorial tumors (table 5):

(*a*) A glioblastoma multiforme should be suspected if there is a considerable amount of focal less than 1 to 2 per second and 2 to 3 per second activity, focal rhythmic discharges at less than 12 per second, little or no focal sharp waves or spikes and few superficial phase reversals.

(*b*) A meningeal tumor is suggested by the presence of a moderate amount of focal less than 1 to 3 per second activity, spread of the abnormality to the oposite side and focal sharp waves despite the absence of a clinical history of epilepsy; the presence of the latter without focal sharp or spike activity is also suggestive.

(*c*) An astrocytoma is indicated by the presence of a considerable amount of focal sharp and spike activity accompanying a history of clinical epilepsy, many superficial phase reversals and relative infrequency of focal less than 1 to 3 per second activity.

Focal 4 to 7 per second activity is the commonest abnormality in all types of brain tumors and may result from local pressure on cortical cells, metabolic changes in these cells or interference with subcortical neuronal pathways.

Acute and severe degeneration of cortical cells, either by direct pressure or as the result of changes in the vascular supply, causes the production of focal less than 1 to 3 per second waves.

Bilaterally synchronous 5 to 6 per second waves were the commonest feature of tumors in and around the third ventricle. The latter also showed bilaterally synchronous 2 to 3 per second waves and bilateral alpha and generalized sharp waves. Interference with corticohypothalamic pathways produces bilaterally synchronous cortical 5 to 6 per second waves.

A focal quiet area may be quite misleading in the localization of an intracranial neoplasm.

Regardless of type, 77 per cent of these supratentorial tumors were correctly localized by the electroencephalogram; 20 per cent were poorly localized, and 3 per cent were localized to the wrong side, in each instance owing to the existence of a quiet area.

TEMPERATURE OF SKELETAL MUSCLE IN CEREBRAL HEMIPLEGIA AND PARALYSIS AGITANS

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VOLUNTARY innervation of the normal striated musculature raises muscle temperature in approximate proportion to the performed external work.[1] Disturbances of skeletal muscle innervation have been found by electromyographic studies in patients with clinical signs of a pyramidal tract lesion or paralysis agitans. The abnormal innervation patterns in these two clinical states may be associated with alterations in temperature of skeletal muscle. This problem has been investigated in a group of subjects without neuromuscular abnormality and patients with chronic unilateral cerebral hemiplegia or paralysis agitans syndrome.

TECHNIC

Temperature measurements were made in 57 experiments on 52 subjects, 18 of whom served as normal controls. The normal controls were ward patients at the Neurological Institute who showed no evidence of neuromuscular abnormality of the upper extremities by history, clinical examination and laboratory tests. Pertinent data on the subjects in the disease groups are given in tables 1 and 2. Standard thermoelectric technic was used for temperature measurements; sensitivity of the circuit allowed a relative precision of temperature measurement of ± 0.01 degree (C.). Needle thermocouples of 40 gage (B. and S.) copper and constantan wire were used in standard 26 gage polished stainless steel tubing. All subjects were in the basal state, nude except for a small sheet over the trunk and reclining prone in an ordinary hospital bed during the experiments. Experiments were begun about 8:00 a.m. and usually lasted three to five hours. Subjects received no medication for at least forty-eight hours prior to the experimental determinations. Most of the temperature determinations were made in the biceps brachii muscle of both sides, the arms being supported free of contact with the bed; the needles were introduced horizontally into the medial aspect of each biceps muscle at two or three points (table 4). Rectal temperatures were measured thermo-

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1. Barcroft, H., and Millen, J. L. E.: The Blood Flow Through Muscle During Sustained Contraction, J. Physiol. **97**:17-31, 1939. Buchthal, F.; Høncke, P., and Lindhard, J.: Temperature Measurements in Human Muscles in Situ at Rest and During Muscular Work, Acta. physiol. Scandinav. **8**:230-258, 1944.

electrically at a depth of 10 cm. In the majority of subjects muscle action potentials were recorded with ink-writing oscillographs by a technic previous described.[2a] In the majority of experiments room temperature was 27.0 to 28.0 C.; range of relative humidity was 45 to 75 per cent; linear air velocity was always below 20 feet (6 meters) per second, no air current being perceptible to the naked skin.

TABLE 1.—*Data on Subjects with Hemiplegia*

Patient	Sex	Age, Yr.	Blood Pressure	Duration of Symptoms, Yr.	Amplitude of Voluntary Movement at Elbow,* Degrees	Spasticity at Elbow, Flexor*	Atrophy of Upper Arm*	Sensory Changes (Entire Side)	Aphasia
1	M	60	140/80	3	0	0	+	Several modalities, slight	Severe expressive
2	F	52	220/120	7	0	++	+	All modalities, slight	0
3	F	62	250/140	1	0	+	++	Several modalities, slight	Paraphasia right-left confusion, finger agnosia
4	M	55	210/110	2	90	++	+	0	Severe expressive, partial receptive
5	F	67	190/90	3	30	++	0	All modalities, slight	0
6	F	58	190/130	1	90	+	+	All modalities, slight	Slight expressive
7	M	68	180/110	4	0	0	++	0	Severe, expressive and receptive
8	M	62	105/70	5	90	++	0	Several modalities, slight	0
9	F	76	180/110	8	0	0	++	0	0
10	F	76	178/95	2	90	+	+	Hyperesthesia to vibration	0
11	F	58	140/96	5	0	++	+	0	Slight expressive
12	F	55	126/118	2	0	++	0	0	Severe expressive and receptive
13	M	55	144/74	1	0	0	0	0	Expressive, receptive
14	F	72	174/86	2	0	0	0	Questionable	Severe expressive and receptive
15	M	72	170/70	1	0	+	0	Questionable	Expressive, severe
16	M	54	170/90	5	180	+	+	Several modalities, slight	0
17	M	52	130/86	6	90	++	+	Several modalities, slight	0
18	M	46	120/68	3	30	+	+	0	0

* Amplitude of voluntary movement at elbow taken as 0 degree when no movement possible, 180 degrees when complete flexion possible. Flexor spasticity at elbow estimated by resistance to passive movement of different rates and amplitudes: 0 = no spasticity, + = moderate spasticity, ++ = severe spasticity. Atrophy of upper arm estimated by inspection and measurement: 0 = no atrophy, + = moderate atrophy, ++ = advanced atrophy. All these subjects had hyperactive tendon reflexes on the affected side and one or more pathologic reflexes. In the majority of cases, reduction in voluntary movement was as marked in the leg as in the arm.

2. (*a*) Hoefer, P. F. A. and Putnam, T. J.: Action Potentials of Muscles in "Spastic" Conditions, Arch. Neurol. & Psychiat. **43**:1-22 (July) 1940; (*b*) Action Potentials of Muscles in Rigidity and Tremor, ibid. **43**:704-725 (Sept.) 1940.

RESULTS

I. *Comparison of Temperatures in Hemiplegia and Paralysis Agitans.*—A. Mean Temperature Differences Between Sides for Individuals (table 3):

The affected side was warmer than the unaffected side in 9 hemiplegic subjects and cooler in 9 subjects (table 3). Only 4 of these differences were statistically significant. The significantly lower temperatures (—0.99 and —0.62 degree C.) occurred in patients with severe atrophy and total paralysis of the limb, but other patients with this same combination of findings had nonsignificant differences between sides. The significantly higher temperatures (+0.75 and +0.42 degree

TABLE 2.—*Data on Patients with Paralysis Agitans*

Patient	Sex	Age, Yr.	Blood Pressure	Origin	Duration, Yr.	Motor Manifestations on Involved Side: Tremor at Elbow*	Motor Manifestations on Involved Side: Rigidity at Elbow*
1	M	36	118/70	Postencephalitic	7	Coarse	+
2	M	50	130/86	Degenerative	2	Coarse	+
3	M	50	128/76	Postencephalitic	20	Coarse	++
4	M	65	136/80	Postencephalitic	20	Coarse	++
5	M	66	140/86	Arteriosclerotic	6	Coarse	++
6	M	45	95/50	Degenerative	5	Coarse	0
7	F	43	110/68	Postencephalitic	15	Coarse	++
8	M	46	120/80	Degenerative	4	Coarse	+
9	M	47	162/92	Degenerative	½	Coarse	+
10	M	27	130/72	Postencephalitic	5	Coarse	+
11	F	58	148/78	Arteriosclerotic	3	Coarse	++
12	M	48	140/76	Postencephalitic	10	Coarse	0
13	M	62	158/84	Postencephalitic	17	Coarse	++
14	F	44	130/74	Degenerative	2	0	+
15	M	35	120/76	Postencephalitic	3	Fine	0
16	F	45	106/62	Degenerative	1	0	+

* Classification of tremor based on that seen during the experimental runs. Fine tremor is barely perceptible to eye or palpating finger; coarse tremor is any whose amplitude is in excess of the fine tremor. Slight rigidity estimated by same technic as spasticity; 0 = no rigidity, + = moderate rigidity, ++ = severe rigidity. No patients were seen with unilateral severe rigidity unaccompanied with tremor. Only patients with grossly unilateral involvement were selected for study.

C.) were present in subjects with no atrophy, 1 subject having a total paralysis of the limb and the other being capable of a 90 degree flexion at the elbow; but other subjects with the same combination of findings showed no significant changes. Of 7 subjects with severe spasticity, 1 had a higher temperature and 6 had lower temperatures in the affected biceps, but none of these changes was significant. Differences in blood pressure between the two arms were less than 20 mm. of mercury in 16 of the subjects and could not be correlated with the temperature differences.

All 16 subjects with paralysis agitans showed higher temperatures on the affected side than on the unaffected, the largest difference

observed being + 1.11 degree C. (table 3). Of these differences only 3 were nonsignificant: +0.09, +0.23 and +0.25 degree C.; these 3 differences occurred in patients who had only barely detectable abnormal motor activity in the affected limb, in subject 15 a very fine tremor (+0.25 degree C.) and in subjects 14 and 16 a very low grade rigidity (+0.09 and +0.23 degree C.). The magnitude of temperature difference between sides was roughly proportional to the intensity of the abnormal motor activity, subjects with the severest combined tremor and rigidity showing the largest temperature differences.

TABLE 3.—*Average Differences in Temperature Between Sides in Subjects of the Three Groups**

Normal Subjects, C.	Subjects with Hemiplegia, C.	Subjects with Paralysis Agitans, C.
+ 0.59	— 0.99 (9)	+ 0.45 (1)
+ 0.42	— 0.62 (7)	+ 1.11 (2)
.....	+ 0.78 (13)	+ 0.56 (3)
— 0.10	+ 0.42 (10)	+ 0.76 (4)
— 0.04	.....	+ 1.06 (5)
— 0.30	+ 0.14 (1)	+ 0.74 (6)
+ 0.12	+ 0.25 (2)	+ 0.89 (7)
— 0.10	— 0.10 (3)	+ 0.62 (8)
— 0.31	— 0.06 (4)	+ 0.43 (9)
+ 0.19	— 0.06 (5)	+ 0.44 (10)
— 0.19	+ 0.18 (6)	+ 0.99 (11)
+ 0.14	— 0.34 (8)	+ 0.42 (13)
— 0.14	+ 0.08 (11)	+ 0.55 (12)
+ 0.02	— 0.01 (12)	.....
+ 0.32	+ 0.05 (14)	+ 0.23 (14)
+ 0.34	+ 0.32 (15)	+ 0.25 (15)
— 0.02	+ 0.16 (16)	+ 0.09 (16)
+ 0.23	— 0.27 (17)	
— 0.21	— 0.30 (18)	

* Each item in the table is the arithmetical mean of all the differences in temperature observed between all pairs of symmetric points in biceps muscle for each subject. Left-sided temperatures have been subtracted from right-sided in the normal series; unaffected side temperatures have been subtracted from affected side temperatures in the two diseased classes. Graphic estimation of the correlation coefficients for temperature differences at different depths of the same level and at different levels of the same depth yielded a value of approximately + 0.5 for all three classes of subjects. Computed standard errors in testing the significance of the average for each subject have been adjusted to allow for the degree of correlation existing between temperature differences at different points in the same subject. The figures in parentheses in columns 2 and 3 refer to the patients listed in tables 1 and 2. In the normal and hemiplegic series, three thermocouples have been employed in each biceps; in the paralysis agitans group, most subjects were explored with two thermocouples in each muscle, a minority with three. Each thermocouple has been read at three different depths of insertion (1.5, 2.5 and 3.5 cm.; consult table 4). The values above the horizontal dotted line in each column are statistically significant.

B. Mean Temperature Differences Between Sides Within Groups (calculated in table 4): For the normal and hemiplegic groups, mean temperature differences between sides were nonsignificant at all experimental points. In the paralysis agitans group, average temperatures at all points on the affected side were significantly higher than on the unaffected side.

C. Mean Temperature Levels Between Groups (table 4): In the hemiplegic subjects average muscle temperatures in both the unaffected and the affected sides and the average rectal temperature were all higher than in the normal series but without statistical significance. These differences in temperature levels between the two groups were shown by subgroup analysis to be correlated with the much higher

TABLE 4.—*Mean Temperatures and Temperature Differences of the Three Groups of Subjects*

Position of Thermocouple	Depth of Measurement, Cm. 1.5	2.5	3.5	Mean Rectal Temperature, C.
Normal Series				
"A" Right biceps	35.05	35.64	35.99	37.12
Left biceps	35.08	35.62	35.87	
	− 0.03	+ 0.02	+ 0.12	
"B" Right biceps	34.91	35.68	35.92	
Left biceps	34.90	35.56	35.80	
	+ 0.01	+ 0.12*	+0.12*	
"C" Right biceps	34.81	35.61	35.89	
Left biceps	35.00	35.54	35.91	
	− 0.19	+ 0.07*	− 0.02*	
Hemiplegic Group				
"A" Affected biceps	35.39	35.85	36.22	37.24
Unaffected biceps	35.36	35.92	36.25	
	+ 0.03	− 0.07	− 0.03	
"B" Affected biceps	35.27	35.93	36.19	
Unaffected biceps	35.30	35.82	36.16	
	− 0.03	+ 0.09	+ 0.03	
"C" Affected biceps	35.08	35.64	36.07	
Unaffected biceps	35.34	35.70	36.09	
	− 0.26	− 0.06	− 0.02	
Paralysis Agitans Group				
"A" Affected biceps	35.84	36.28	36.63	37.09
Unaffected biceps	35.09	35.92	36.22	
	+ 0.73	+ 0.36	+ 0.41	
"B" Affected biceps	35.63	36.32	36.60	
Unaffected biceps	35.11	35.50	36.12	
	+ 0.52	+ 0.82	+ 0.48	

Each value in the table is the arithmetical mean of the measurements on all the subjects in each group at the designated depth and level. Values for the mean temperature difference at each level and depth were calculated by subtracting the left-sided values from the right-sided values in the normal series; in the two disease groups the mean temperature differences were calculated by subtracting values on the unaffected side from corresponding values on the affected side. Statistical significance was evaluated by small sample technic. For the normal and the hemiplegic series, three thermocouples ("A," "B" and "C") were placed in each biceps muscle in the paralysis agitans group, most subjects were explored with two thermocouples ("A" and "B") and so "C" values are not reported for this group. Position "A" was at the junction of the proximal and distal portions of the arm; "B," at the midpoint of the arm; "C," at the junction of the middle and distal portions of the arm. Three different depths of insertion are 1.5, 2.5 and 3.5 cm. for each thermocouple. Figures of tables 3 and 4 were computed from the same body of experimental data.

incidence of arterial hypertension in the hemiplegic group; therefore on the basis of the available data the hemiplegia itself cannot be the only physiologic variable which may be related to the higher mean thermal

levels in the disease group. In the paralysis agitans group mean temperatures at all points on the affected side were significantly higher than on either side in the normal series. In addition, at most points on the unaffected side in the paralysis agitans group, mean temperatures were higher than in the normal series but not significantly; this finding is probably related to the fact that the grossly uninvolved side in paralysis agitans showed some minor clinical or electromyographic involvement in 13 of the 16 patients. Because of the higher muscle temperature levels in the paralysis agitans group the rectal–mean muscle temperature differences were significantly smaller than in the other two groups. The problems raised by the radial and longitudinal temperature gradients of

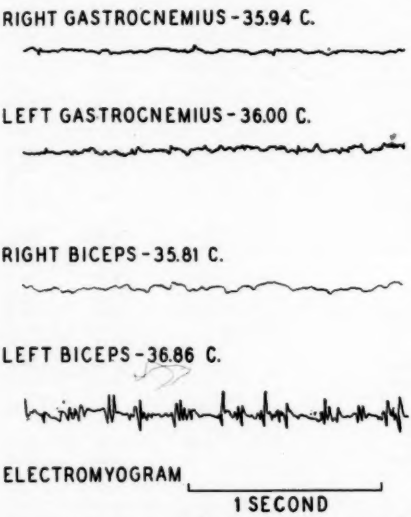

Fig. 1.—Temperature and electrical activity in right and left gastrocnemius and biceps muscle of a patient with paralysis agitans. The patient clinically displayed coarse tremor and rigidity of the left biceps and minimal clinical signs in the other three extremities. Note the gross elevation of temperature in the left biceps with the electrical bursts corresponding to tremor activity. Temperature values are the means for three thermocouples in each muscle. Surface electrodes were used.

table 4 have been separately analyzed in detail for group of normal subjects.[3]

II. *Effect of Abnormal Motor Activity on Temperature Level.*—A. Paralysis Agitans Subjects: The following intraindividual data support the already drawn conclusion that elevation of temperature in paralysis agitans is proportional to the intensity of the abnormal motor activity (section I, A).

3. Pennes, H. H.: Analysis of Tissue and Arterial Blood Temperatures in the Resting Human Forearm, J. Applied Physiol. **1**:93-122, 1948.

1. Several subjects in whom only one extremity showed an excess of abnormal motor involvement had a great elevation of temperature only in this affected extremity as compared with the 3 uninvolved extremities (fig. 1).

2. In 5 subjects with alternating tremor and with rigidity, simultaneous determinations were made in two pairs of protagonist-antagonist muscles (biceps-triceps and forearm extensor–flexors); the temperatures of all the abnormally active muscles were grossly elevated as compared with the opposite, uninvolved, extremity (value for biceps, tables 3 and 4 are typical).

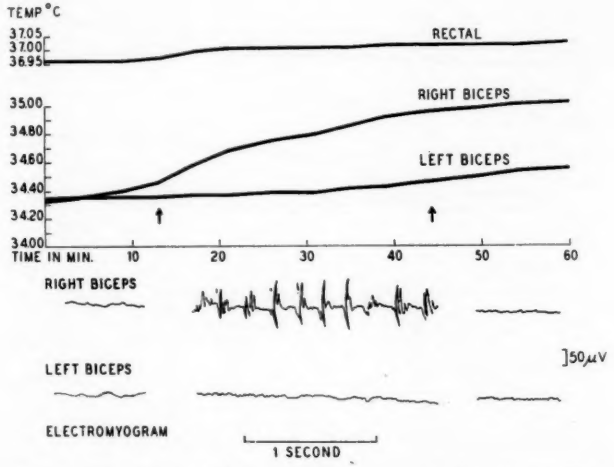

Fig. 2.—Temperature and tremor activity in paralysis agitans. The patient (subject 12) clinically displayed regular coarse tremor at the left elbow at a 6 per second rate without evidence of rigidity; there was no clinical or electrical activity of the right arm. The control period before the first arrow was without apparent clinical tremor or recorded electrical activity; between the two arrows a spontaneous coarse, regular tremor of the left elbow is evident; there was spontaneous disappearance of the tremor and electrical activity after the second arrow. Note the progressive rise in temperature of the left biceps muscle during the period of muscle activity. Temperature values are the means for three thermocouples in each muscle. Surface electrodes were used.

3. Second experiments were done on 5 patients several weeks after the first determinations. During the first run significant differences in temperature between the two sides had been found in all these subjects. Two of the patients reported themselves as "relaxed" at the start of the second determination, showing no difference in clinical or electrical activity between limbs; no significant temperature changes were present in these 2 subjects in the second experiment. The 3 patients who

showed motor differences between sides in the second experiment again had significant elevations on the affected side.

4. The "spontaneous" intermittency of abnormal motor activity so commonly seen in these patients [4] provided the most direct evidence relating the increased temperature to intensity of abnormal motor activity (figs. 2 and 3). In subjects with tremor, the temperatures underwent cyclic elevations whose peaks averaged 0.1 to 0.3 degree C.; mean temperature level during the cyclic changes was also elevated. The cyclic thermal elevations coincided in time with the bursts of tremor activity. Because of this inherent variation in motor activity in paralysis agitans, steady temperature readings were more difficult to obtain than in hemiplegia.

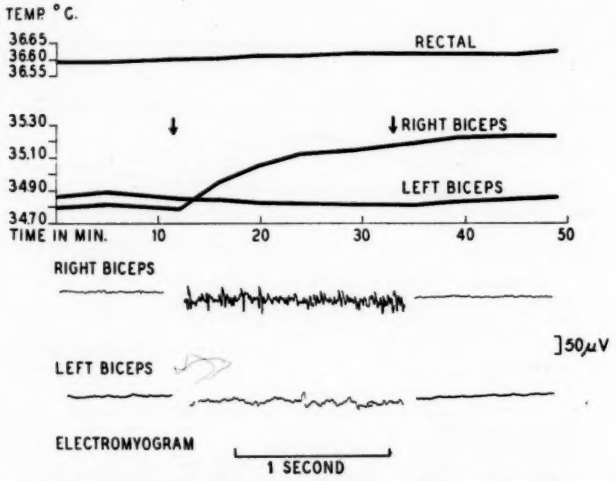

Fig. 3.—Temperature and rigidity in paralysis agitans. The patient clinically had a low grade rigidity in the right biceps muscle without tremor; there was no abnormal motor activity of the left arm. There was no electrical activity before and after the arrows; irregular, low voltage pattern appeared spontaneously between the arrows. Note the progressive rise in temperature in the right biceps muscle during the period of electrical activity. Temperature values are the means for two thermocouples in each arm. Needle electrodes were used.

The values in tables 3 and 4 for paralysis agitans are therefore partially influenced by the relative rarity of a stable motor level.

Quantitative comparison cannot be made of the temperature changes produced by tremor or rigidity as separate mechanisms. This follows from the high incidence of combined tremor and rigidity in the same limb and the inherent difficulties in the quantitative estimation of rigidity by either clinical or electrical technics. Despite these restrictions, several

4. Wilson, S, A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940, vol. 2.

conclusions are valid: (*a*) Either tremor or rigidity alone, beginning after a period of clinical inactivity and electrical silence, produced progressive temperature rises in muscle (figs. 2 and 3). (*b*) The 2 subjects with low grade rigidity as their only motor manifestation did not have significant temperature changes during the entire experiment; 2 with coarse tremor and no rigidity did show significant temperature elevations. The quantitative factor is probably crucial; for example, subject 15 with barely perceptible tremor did not have a significant difference (+ 0.25 degree C.) between sides. In addition, an uncontrollable time factor

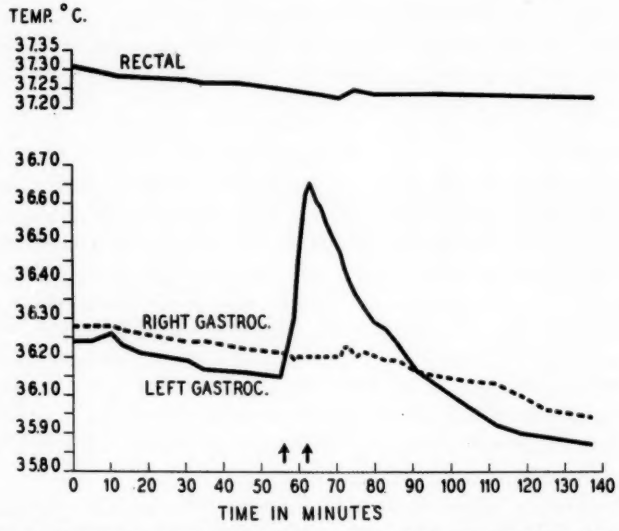

Fig. 4.—Temperature and ankle clonus in hemiplegia. The patients had chronic hemiplegia. There was no muscle activity of the left leg without stimulation. Between arrows, a rapid, moderate amplitude ankle clonus was induced and maintained on the left by slight upward pressure on the sole. Note the sharp rise in temperature of the left gastrocnemius muscle with the onset of ankle clonus. Temperature values are the means for two thermocouples in each muscle.

enters into consideration: With prolongation of the period of muscle activity, the subject of figure 3 with rigidity might easily have shown a final elevation of temperature comparable to that seen with coarse tremor. Since severe rigidity was always associated with coarse tremor the effects of the former could not be evaluated separately.

B. Hemiplegic Subjects: 1. Changes of sufficient magnitude in the external motor activity of the hemiplegic limb were associated with rises in temperature; figure 4 is representative of the effect of induced ankle clonus in 4 subjects. One patient with a rhythmically repeated

spontaneous "mass reflex" activity of the leg showed a 0.26 degree C. rise over a twenty-five minute period.

2. Confirmatory of the observations of Hoefer,[5] many of these subjects demonstrated no action potentials from the biceps muscle with either surface or coaxial needle electrodes at usual standards of amplification, even with the elbow in a spontaneously assumed position of flexion with an internal angle of 90 degrees or less. However, half the subjects showed intermittent action potentials from the affected biceps muscle which disappeared with a slight (10 to 20 degrees) induced adjustment of the elbow; during these periods of spontaneous electrical activity minor temperature rises of about 0.1 degree C. were sometimes detected. Several patients had spontaneous elbow movement accompanying such acts as sneezing or yawning; at these times small (0.1 degree C.) cyclic thermal rises also occurred.

COMMENT

The resting normal human musculature shows no electrical activity [5] and is therefore considered to be without innervation from the central nervous system. In this study abnormal innervation of the striated musculature, independently of the particular neurophysiologic mechanism in operation, has been found sufficient to raise local muscle temperature. This finding forms a parallel to the fact that voluntary innervation of skeletal muscle by normal persons also elevates muscle temperature.[1] The thermal changes in all these cases must be related to alterations in the local rate of heat production and volume circulation of the blood; quantitative analysis of these factors is presented elsewhere for a group of normal subjects in the resting state.[3]

Muscle temperature in paralysis agitans is raised above normal in rough proportion to the intensity of the abnormal motor activity. The "basal" motor state in this disease is one of continuous or practically continuous involuntary muscle activity with resulting elevation of the average thermal level. In normal subjects the temperature of exercising local forearm muscle can be raised almost to or above the rectal temperature [1b]; likewise, in paralysis agitans, the muscle-rectal temperature difference (for the active muscles) is significantly reduced because of elevation of muscle temperature. In generalized muscular exercise, rectal temperature shows a rise beginning during the period of exercise.[6] At least two factors may contribute to the normal rectal temperatures found in paralysis agitans: (*a*) involvement of insufficient muscle mass in the

5. Hoefer, P. F. A.: Physiology of Motor Innervation in the Dyskinesias, A. Research Nerv. & Ment. Dis., Proc. **21**:502-528, 1941.

6. Bainbridge, F. A.: Physiology of Muscular Exercise, London, Longmans Green & Company, 1931, chap. 29.

abnormal motor activity, since in most of these cases the disease was grossly unilateral or involved principally one extremity; (*b*) the possibility of increased heat dissipation by compensatory mechanisms.

Brief and transient signs of innervation in the hemiplegic "spastic" limb are accompanied with short thermal rises, but it is significant that for the limb in mechanical rest and without electrical activity no such temperature changes were detected. At least four factors contribute to the fact that the "spastic" limb at rest shows no thermal deviation from normal: (*a*) the low or absent innervation of the "spastic" biceps, unlike the situation in rigidity, in which abnormal innervation takes a tonic form [2b]; (*b*) cancellation of theoretic thermal effects of "spasticity" by possibly counteracting disturbances, such as muscle atrophy, partial or total muscle paralysis or disuse, sensory changes and vasomotor disturbances of central origin caused by the lesion; (*c*) possible reduction of blood flow through the "spastic" muscle if a state of sustained contraction really does exist; (*d*) the maintenance of the theoretic "spastic" contraction at a low metabolic rate of muscle, although no consistent alteration of basal metabolic rate has been found in hemiplegic subjects with varying degrees of flaccidity and "spasticity."[7]

SUMMARY

1. The majority of hemiplegic subjects had nonsignificant temperature differences between the right and the left biceps muscle. When significant differences existed, they could not be ascribed exclusively to any one gross alteration of neurophysiologic function in the limb. Hemiplegic subjects did show transient rise in muscle temperature accompanying temporary innervation of the limb.

2. The majority of patients with unilateral paralysis agitans had significant temperature elevations on the affected side when the motor involvement exceeded certain clinically defined limits. The rise of temperature in paralysis agitans varied as the level of activity of the affected musculature.

Dr. Paul Hoefer provided the electromyographic equipment and assisted in interpretation of records; Dr. John Fertig assisted in the statistical analyses.

7. Ellis, L. B., and Weiss, S.: Vasomotor Disturbance and Edema Associated with Cerebral Hemiplegia, Arch. Neurol. & Psychiat. **36**:362-372 (Aug.) 1936.

USE OF POTASSIUM IN PROTRACTED INSULIN COMA

Preliminary Report

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THE PROBLEM of protracted coma is one which faces most institutions that undertake to treat psychotic patients with insulin. According to Lester,[1] it occurs once in every 1,887 normal comas. Its seriousness appears fairly obvious when thorough studies and proper clinical evaluation of the patient are undertaken and the resultant mortality and complications reviewed. Therapy of protracted coma, however, has been indefinite and controversial. The approaches in handling the problem have been manifold. The purpose of this paper is to add further to the reported cases of protracted coma and to present a relatively new mode of therapy with a possible explanation for its use. It is our aim to present the course of 2 patients in protracted coma and to indicate fully our mode of therapy for each and then to present an outline of therapy for patients in such clinical states.

The state of protracted coma occurring during insulin therapy is characterized by several dominant features, all of which vary from patient to patient: (1) a normal blood sugar level and/or hypoglycemia; (2) a state of dehydration and disturbed electrolyte balance; (3) a disturbance in the sympathetic and the parasympathetic function and balance; (4) a neurologic syndrome which varies in accordance with the different stages described by Himwich[2] during the course of hypoglycemic coma; (5) a failure to respond to the routine methods of therapy for hypoglycemic coma, and (6) a recovery phase characterized by the presence of an organic syndrome, a Korsakoff-like psychosis of varied duration.

From the Department of Neurology and Psychiatry, Albany Hospital and Albany Medical College.

1. Lester, D.: Study of Prolonged Coma Following Insulin Shock, Am. J. Psychiat. **95**:1083 (March) 1939.

2. Himwich, H. E.: The Physiology of the (Shock) Therapies, Psychiat. Quart. **18**:357 (July) 1944.

The diagnosis of protracted coma in our cases has been made when a patient has failed to recover from coma following the administration of what is thought to be adequate amounts of dextrose (each patient received a minimum of 125 Gm. intravenously in a 25 per cent solution).

REPORT OF CASES

CASE 1.—J. W., a 34 year old white married woman, was admitted to the psychiatric ward of the Albany Hospital on Feb. 27, 1945, with a diagnosis of postpartum psychosis—schizophrenia. The past history was essentially noncontributory except for the report of one convulsion which occurred two years before admission. The family history was noncontributory. Conditions observed on physical and neurologic examinations were essentially normal. Insulin therapy was instituted on the second day after admission, at which time the patient received 25 units of regular insulin at 6 a.m. The amount of insulin was increased by 25 units daily until she received a total of 100 units daily at 6 a.m.

On the fifth day of treatment, the patient was given 100 units of regular insulin, and one hour and forty-five minutes after its administration she began to manifest signs of hypoglycemia. She became drowsy and exhibited profuse diaphoresis and clonic spasms. One hour after the onset of the hypoglycemic symptoms, an attempt was made to bring her out of insulin shock. She was given 2,000 cc. of sweetened grapefruit juice by gavage. At that time the pulse rate was 64, as contrasted with the variation of 80 to 96 per minute during the varied phases of hypoglycemia. Despite the administration of dextrose, the patient failed to respond. She was restless, struggled and bit her tongue several times, although such behavior was not to be confused with any semblance of a convulsive pattern.

Fifteen hundred cubic centimeters of a 25 per cent solution of dextrose in distilled water was administered intravenously without therapeutic response. The blood sugar, nonprotein nitrogen and serum potassium levels were obtained (subsequent study of which revealed blood sugar, 510 mg., nonprotein nitrogen, 27 mg., and potassium, 15.4 mg., per hundred cubic centimeters).[3] The patient began to manifest tachypnea, dyspnea and hyperpnea. She was given 1 cc. of epinephrine hydrochloride (1:1,000) intramuscularly, and administration of oxygen was started through a nasal catheter at a rate of 5.5 liters per minute. She failed to respond and began to vomit dark brown material. At 11:30 a.m., the patient was given 200 mg. of thiamine hydrochloride intravenously without immediate effect. At 12:15 p.m., the pulse rate had risen to 128; at 1:15 p.m., the systolic blood pressure had fallen to a level of 75. Throughout the rest of the afternoon, the patient was overactive and restless. At 4 p.m., she had a temperature of 103.4 F. The pulse rate was 112; the respiration rate, 22, and the blood pressure, 100 systolic and 70 diastolic. Shortly before these values were obtained, she had received 2 cc. of parentosol B® (a vitamin B preparation) intramuscularly and a subfascial infusion of 1,000 cc. of 5 per cent dextrose in distilled water.

At 4:30 p.m., administration of potassium chloride, 2 Gm. every two hours by gavage, was started. The temperature and pulse rate subsequently returned to normal, and the blood pressure was maintained at normal level. Two and

3. The flame photometer technic was used, with an evaluated accuracy of ± 5 per cent.

one-half hours after the initial dose of potassium chloride, the patient responded verbally and showed the first evidence of reversibility of the protracted coma, the total duration of which had been twelve hours. She manifested a Korsakoff-like psychosis for thirty-six hours from the time of the onset of hypoglycemia. Insulin therapy was discontinued, and five days after the protracted coma she was discharged without improvement in the psychiatric state.

CASE 2.—M. R., a 21 year old single white woman, was admitted to the psychiatric ward of the Albany Hospital on Oct. 4, 1945, with a diagnosis of schizophrenia. The family history revealed hospitalization of a paternal uncle because of mental illness. The past history revealed the presence of a cardiac murmur discovered one year prior to her admission to this hospital. The physical examination disclosed nothing abnormal except a loud blowing systolic murmur heard best at the apex but transmitted over the entire precordium and to the left axilla and posterior area of the chest. The neurologic examination revealed grossly normal conditions. The day after admission, therapy with regular insulin, 25 units, was started and the dose was increased by 25 units daily until the patient received a total daily dose of 200 units of regular insulin. She was also treated with electric convulsion therapy simultaneously and received electric shock treatment every other day. On the thirteenth day of treatment, the patient received 200 units of regular insulin at 6 a.m. to initiate her seventh coma. At 8:15 a.m., she began to manifest the first signs of hypoglycemia and exhibited marked diaphoresis, greatly dilated pupils and muscular tremors and twitches. At 8:30 a.m. her pupils were fixed; there were bilaterally positive Babinski signs and bilaterally sustained ankle clonus. At 9 a.m. a lowered pulse rate was noted, being at that time 68 per minute and irregular. In addition, the patient's breathing was stertorous.

An attempt was made to reverse the hypoglycemic state. The patient was given dextrose, 250 Gm. in a 25 per cent solution, but she failed to respond. At 10.15 a. m., she was given solu-B, sterile® (a vitamin B preparation), 20 cc., intravenously, without immediate response. The pulse rate at that time was 78 and regular. The pupils were dilated, and Babinski signs bilaterally were positive. At 11 a. m., an intravenous infusion of dextrose, 5 per cent, in isotonic sodium chloride solution was started. At 11:30 a. m., on the basis of our previous experience, we decided to give this patient potassium chloride, this time intravenously. She was given potassium chloride, 1 Gm. intravenously over a twenty minute period. Five minutes after the administration of the drug, the patient responded verbally. She was then given 2 Gm. of potassium chloride by mouth for three doses. The response following the intravenous administration of potassium chloride was dramatic. Insulin therapy, with 175 units of regular insulin daily, was resumed three days later without untoward sequelae. The protracted coma produced no effect on the clinical progress of the patient.

COMMENT

That disturbed carbohydrate metabolism is not the sole factor in protracted coma is fairly apparent from the observations that these patients failed to respond despite adequate administration of dextrose. Disturbances in other phases of metabolism must occur. Changes in water metabolism take place, in view of the marked diaphoresis which most patients manifest in insulin coma. Dehydration is a significant

element, and with it are the associated changes in electrolyte balance both extracellular and intracellular, such changes having recently been reemphasized by Darrow.[4] The significance of electrolyte equilibrium, particularly with reference to potassium in diabetic acidosis, has been observed by several investigators.[5]

From available data, it is shown that certain significant changes occur during the course of hypoglycemia induced by insulin. Harris and his co-workers [6] noted that a marked lowering of serum potassium occurred in certain patients during the administration of insulin. They felt that coma was deeper and shock severer in patients with lower potassium levels than in others. Beiglboeck and Dussik [7] reported a lowered serum potassium level during hypoglycemia. Clegg [8] stated that the resting potassium fluctuates, but always above the normal level; during coma the potassium tends to fall below its precoma level. In discussing the pathologic damage associated with insulin hypoglycemia, Yannet [9] emphasized that insulin itself and not anoxia was responsible for the demonstrable pathologic change. He noted that in dogs subjected to hypoglycemia for a considerable period a loss of cellular potassium occurred, with a resultant replacement with sodium and water. Georgi [10] noted that serum potassium fell during insulin hypoglycemia. Ashford and Dixon [11] showed by studying brain tissue in vitro that

4. Darrow, D. C.: Disturbances in Electrolyte Metabolism in Man and Their Management, Bull. New York Acad. Med. **24**:147 (March) 1948.

5. Atchley, D. W., and others: On Diabetic Acidosis: Detailed Study of Electrolyte Balance Following Withdrawal and Re-Establishment of Insulin Therapy, J. Clin. Investigation **12**:297 (March) 1933. Holler, J. W.: Potassium Deficiency Occurring During Treatment of Diabetic Acidosis, J. A. M. A. **131**: 1186 (Aug. 10) 1946. Martin, H. E., and Wertman, M.: Serum Potassium, Magnesium, and Calcium Levels in Diabetic Acidosis, J. Clin. Investigation **26**:217 (March) 1947.

6. Harris, M. M., and Horwitz, W. A.: Metabolic Studies of Mental Patients Treated with Insulin Hypoglycemic Shock Treatment (Potassium Tolerance Before and After Treatment), Psychiatric Quart. **13**:429 (July) 1939. Harris, M. M.; Blalock, J. R., and Horwitz, W. A.: Metabolic Studies During Insulin Hypoglycemia Therapy of Psychoses, Arch. Neurol. & Psychiat. **40**:116 (July) 1938.

7. Beiglboeck, W., and Dussik, T.: Physiology of Hypoglycemic Shock in Treatment of Schizophrenia, Am. J. Psychiat. (supp.) **94**:50 (May) 1938.

8. Clegg, J. L.: Serum-Potassium and Serum-Calcium in Insulin Shock Therapy, Lancet **1**:871 (April 15) 1939.

9. Yannet, H.: Effect of Prolonged Insulin Hypoglycemia on Distribution of Water and Electrolytes in Brain and in Muscle, Arch. Neurol. & Psychiat. **42**:237 (Aug.) 1939.

10. Georgi, F.: Humoralpathologische Bemerkungen zur Insulinschock-Therapie bei Schizophrenen, Schweiz. Med. Wchnschr. **66**:935 (Sept. 26) 1936.

11. Ashford, C. A., and Dixon, K. C.: Effect of Potassium on Glucolysis of Brain Tissue with Reference to Pasteur Effect, Biochem. J. **29**:157, 1935.

the Pasteur effect for depression of carbohydrate metabolism, under aerobic as compared with anaerobic conditions, could be inhibited by the addition of potassium salts. Cantarow and Trumper [12] noted a lowering of serum potassium in normal and diabetic subjects following the administration of insulin.

The role of potassium in the central nervous system has been widely described. Vogt [13] and Brown and Feldberg [14] also Feldberg and Guimarais [15] have demonstrated the role of potassium in the liberation and action of acetylcholine. Welsh and Hyde [16] offered the same opinion.

Pudenz and his co-workers [17] proved that the potassium administered in the treatment of familial periodic paralysis was taken up not by the muscle cells but by the cells in the central nervous system. The use of potassium salts in neuralgia [18] and in visceralgia [19] has been reported. Maidan-Maidansky [20] utilized potassium permanganate in the treatment of patients with paralysis agitans. Patients with myasthenia gravis had likewise been treated with potassium compounds before the advent of neostigmine (prostigmin®) and the reciprocal effects of the two drugs studied.[21] Hirschfelder and Haury [22] reported the variations in magnesium and potassium in essential epilepsy. The effects

12. Cantarow, Abraham, and Trumper, Max: Clinical Biochemistry, ed. 3, Philadelphia, W. B. Saunders Company, 1945, p. 246.

13. Vogt, M.: Potassium Changes in Stimulated Superior Cervical Ganglion, J. Physiol. **86**:258 (March) 1936.

14. Brown, G. L., and Feldberg, W.: Action of Potassium on Superior Ganglion of Cat, J. Physiol. **86**:290 (March) 1936.

15. Feldberg, W., and Guimarais, J. A.: Liberation of Acetylcholine by Potassium, J. Physiol. **86**:306 (March) 1936.

16. Welsh, J. H., and Hyde, J. E.: Effects of Potassium on Synthesis of Acetylocholine in Brain, Am. J. Physiol. **142**:512 (Nov.) 1944.

17. Pudenz, R. H.; McIntosh, J. F., and McEachern, D.: Role of Potassium in Familial Periodic Paralysis, J. A. M. A., **111**:2253 (Dec. 17) 1938.

18. Mamontoff, N. I.: Treatment of Neuralgia with Potassium Iodide, Vrach. delo. **11**:1425 (Sept.) 1928.

19. Simforoff, E. F.: On Subcutaneous Injections of Potassium Iodide and Sodium Iodide in Treatment of Visceralgia, Klin. Med. **6**:1310, 1928.

20. Maidan-Maidansky, E. M.: Potassium Permanganate for Treating Paralysis Agitans, Mosk. med. j. **8**:30, 1928.

21. Cumings, J. N.: Role of Potassium in Myasthenia Gravis, J. Neurol., Neurosurg. & Psychiat. **3**:115 (April) 1940. Thompson, V., and Tice, A.: Action of Drugs Beneficial to Myasthenia Gravis: Effect of Prostigmine and Guanidine on Serum and Muscle Potassium, J. Pharmacol. & Exper. Therap. **73**:455 (Dec.) 1941.

22. Hirschfelder, A. D., and Haury, V. G.: Variations in Magnesium and Potassium Associated with Essential Epilepsy, Arch. Neurol. & Psychiat. **40**:66 (July) 1938.

and the role of potassium have been studied in the normal physiology of muscle [23] and in various disease states.[24]

It is of considerable interest to note that in recent reports on the crush syndrome death has been attributed to increased serum potassium which subsequently produces cardiac arrest. Successful therapy undertaken to reduce the potassium level has included the use of insulin and dextrose.

Cleckley and Templeton [25] have reported the only known case of protracted coma in which marked therapeutic response followed the administration of 2 Gm. of potassium chloride orally.

On the basis of these data, it was thought advisable to administer potassium in an attempt to produce reversibility in protracted coma. In view of the relatively dramatic responses obtained in only 2 cases and in view of the relatively undefined role of potassium in the physiology of the body, it was considered advantageous to submit this preliminary report. That pronounced shifts in serum potassium level are not necessary for the production of pathologic syndromes is apparent from the work of Pudenz. A shift of only 10 per cent from normal is apparently enough to bring on attacks of familial periodic paralysis in susceptible persons. It is not necessary to have a loss of potassium from the body, for in familial periodic paralysis potassium secretions remain unchanged. That serum potassium levels are not an accurate index of tissue potassium, the concentrations of which are physiologically important, is likewise an accepted fact.

It is not our intention to attribute the therapeutic responses obtained solely to the use of potassium or to say that a direct correlation beween the two exists. Some changes, however, are initiated by the administration of potassium, particularly when given intravenously. This is the first known report of a case of protracted coma in which the patient was treated by the intravenous administration of potassium. The nature of the initiated changes remains a problem for study. Is potassium merely a reflection of disturbed cellular physiology of the central nervous system, or is it necessary for physiologic shifts of potassium to occur to promote recovery? Further studies are now being carried out in an attempt to answer such questions.

The intravenous administration of potassium must be handled with caution. The cardiac effects of potassium are well established, and

23. Hoff, H. E.; Winkler, A. W., and Smith, P. K.: Recovery of Fatigued Muscle Following Intravenous Injection of Potassium Chloride, Am. J. Physiol. **131**:615 (Jan.) 1941.

24. Cumings, J. N.: Potassium Content of Muscle in Disease, Brain **62**:153 (June) 1939.

25. Cleckley, H., and Templeton, C. M.: Prolonged Coma in Insulin Therapy of Psychoses, Am. J. Psychiat. **97**:844 (Jan.) 1941.

during the course of administration of potassium discernible changes occur. There is definite lowering of the cardiac rate with alteration in rhythm, most commonly a dropped beat. Transient electrocardiographic changes likewise occur. It is our practice to administer potassium, 10 per cent solution, in a 1 cc. tuberculin syringe with constant auscultation of the heart during administration of the drug. The material is injected very slowly, at the rate of 0.02 to 0.04 Gm. at a given injection; another injection is not given until cardiac rhythm is reestablished. Calcium for intravenous injection is available at the bedside to counteract any side reactions which may ensue. We have administered potassium intravenously on repeated occasions since its use in the 2 cases reported here, and no untoward signs or symptoms have appeared. Winkler and his co-workers [26] have reported the following critical levels: Fifty to 60 mg. per hundred cubic centimeters produces cardiac arrest, while 20 to 30 mg. produces electrocardiographic changes. It is of interest to note that with the use of potassium, critical concentrations are rarely reached.

From available data, a fundamental regimen for protracted coma should include adequate administration of dextrose by the intravenous route and adequate administration of electrolytes, particularly potassium. It is deemed advisable to administer potassium prophylactically before insulin treatment by the use of potassium chloride, 2 Gm. four times a day during the course of insulin therapy.

SUMMARY

Two cases of protracted insulin coma are reported.

The use of potassium in protracted coma is reported, and the first clinical report of intravenously administered potassium in the therapy of protracted coma is presented.

An outline of treatment for protracted coma is offered.

In the 2 cases recorded, the protracted coma produced no discernible effect on the clinical progress of the patient.

26. Winkler, A. W.; Hoff, H. E., and Smith, P. K.: Electrocardiographic Changes and Concentration of Potassium in Serum Following Intravenous Injection of Potassium Chloride, Am. J. Physiol. **124**:478 (Nov.) 1938.

A POSSIBLE PSYCHOLOGIC COMPLICATION AND CONTRAINDICATION TO ELECTRIC SHOCK THERAPY MODIFIED WITH CURARE

Report of a Case

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THE WIDE application of electric shock therapy and its modifications, such as curarization, has demanded careful evaluation of its complications and contraindications. Attention has been directed primarily to the problem of the somatic complications of shock therapy (with and without curare), as well as to the definition of the limits of somatic tolerance (contraindications) to these treatments.[1] Because of the rigors of shock therapy, there is a very real justification for this preoccupation with somatic sequelae and contraindications.

There has been no similar definition of the psychologic complications and contraindications to electric shock therapy or its modifications, at least as reflected in the psychiatric literature. Most studies have been conducted on "organic reaction patterns" following shock therapy, but these studies are largely within the frame of the search for somatic complications. Frosch and associates[2] have reported acute psychotic reactions following electric shock but have not considered them in terms of contraindication.

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1. Osgood, C. W.: Unusual Reactions to Electric Shock, J. Nerv. & Ment. Dis. **100**:343 (Oct.) 1944. Lowinger, L., and Huddleson, J. H.: Complications in Electric Shock Therapy, Am. J. Psychiat. **102**:594 (March) 1946. Pacella, B. L., and Barrera, S. E.: Sequelae and Complications of Convulsive Shock Therapy, Arch. Neurol. & Psychiat. **53**:82 (Jan.) 1945.

2. Frosch, J.; Impastato, D. J.; Ottenheimer, L., and Wortis, S. B.: Some Reactions Seen after Electric Shock Treatment, Am. J. Psychiat. **102**:311 (Nov.) 1945.

The following report of a case is submitted for its interest as an instance of a psychologic complication developing in reaction to electric shock therapy modified by curare. It is also felt that this report may point to a possible psychologic contraindication to electric shock therapy with curarization for patients showing dynamic defenses of the type described in this case.

REPORT OF CASE

History.—A white married man, aged 27, veteran of World War II, first exhibited psychotic symptoms in 1944, while he was stationed in New Jersey awaiting shipment overseas. Shortly after being alerted for overseas duty, he became suspicious of his wife and accused her of sexual infidelity with other soldiers. He engaged her in a fight, in which she was able to overpower him, much to his chagrin. At his overseas station in England the patient felt abused by his first sergeant and retaliated by brooding sulkily. On one occasion he was the active homosexual partner of another soldier and reacted with intense fear, guilt and confusion after the act. He then reported repeatedly on sick call, demanding to be placed in hospital. He became hostile and suspicious of the doctors attending him on sick call and because of these paranoid attitudes was placed in a neuropsychiatric ward of an evacuation hospital. There he developed much shame and anger over his being classified as a psychiatric casualty.

After evacuation to the United States, he was discharged because of his mental illness, as well as rheumatoid arthritis of both hip joints. His readjustment to civilian status was inadequate. He reacted to the birth of a son with bitter resentment toward his wife and the baby. Preoccupation with somatic function then developed into frank delusions of "bones rotting, brain getting moldy and body disintegrating." In November 1946, he suddenly lapsed into a stupor, after a violent trembling episode. He was then admitted to a Veterans Administration hospital, where he was inaccessible, usually dejected, occasionally assaultive, sometimes careless about excreta, severely blocked and suspicious. He vaguely discussed regret over being married, shame about his being a mental case and suicidal thoughts.

The patient was the youngest of six children, born in a coal-mining town in Pennsylvania. The father had been a coal miner, of Polish extraction. He was an indolent, quiet, passive person who resented his poor financial status, but who could not bring himself to do anything constructive about it. Periodically the father would drink heavily and, while intoxicated, physically abuse his wife. The patient felt that his father was uninterested in any of the children save the eldest, Joe. When the father's attention was focused on him, it was usually in an ill tempered, threatening manner. After an illness of six months, the father died of cardiac decompensation, when the patient was 9 years of age.

The patient's mother, aged 68, still living, was born in the Ukraine. She dominated her children and husband by exhibiting "hysterical fits during which she'd scream, cry and pull out her hair." As a child, he recalled being in terror over the possibility of one of mother's "fits." After the father's death, the patient slept with the mother each night until he was 12 years old. The mother always stressed his immaturity, and at the time of his marriage she objected because he was "too much of a child."

After the father's death, the patient's oldest brother, Joe, assumed the paternal role in the family. He invoked a strict discipline on the other children and

enforced it with sadistic punishments for any infractions of his rules. The patient always felt inferior to this brother in strength, size, self respect, self confidence and intelligence and resented him bitterly. This resentment was not expressed verbally for fear of the brother. The same older brother engineered the patient's marriage to his (Joe's) sister-in-law.

The patient's four older sisters had exhibited serious emotional illnesses. The oldest sister had been sexually delinquent and promiscuous. The next older sister had been treated for a schizophrenic reaction. The other sisters had unsuccessful marriages and work records. Each of the sisters was uninterested in and hostile toward the patient and resented maternal attention given him during childhood. Since the sisters were less threatening to him than Joe, he sought their company as a child.

As a young child, the patient was shy, timid and extremely fearful. He clung desperately to his mother for protection from the brother and father. The mother at times would refuse him such protection because of her own fears. In school, which he attended through twelve grades, he continued to be timid and suspicious and became seclusive and sensitive.

During adolescence, he felt ashamed of his small stature. "I was afraid of becoming 21 because I knew I would stop growing then." He compensated partially for this feeling by trying to excel in his studies at high school. Imperfect school performance depressed him considerably.

After graduation from high school he was disappointed in and felt humiliated by jobs for the Works Progress Administration and in factories. He rebelled against supervision on his jobs and was discharged several times for sulking insubordination.

His psychosexual development was confused and frightening. An early memory involved his feeling embarrassed and guilty over witnessing parental intercourse when he was 7 years old. Shortly thereafter, and until puberty, he indulged in homosexual acts with boys of his age, always experiencing anxiety and guilt. Masturbation started at puberty and has continued. He dated no girl until he was 21, when he met his brother's sister-in-law, whom he subsequently married. Premarital attempts at intercourse were unsuccessful, clumsy and guilt-laden fiascos; because of these trials the patient felt obligated to marry the girl and resentful about being so trapped. Guilt over marital intercourse had contributed to further sexual frustration. The patient's wife also had undiminished sexual guilt feelings after marriage and was therefore unable to reassure him in this regard.

Course in Hospital.—On his admission to a Veterans Administration hospital, his condition was diagnosed as paranoid schizophrenia, and he was given a course of eight electric shocks, which led to no permanent change in his behavior. Several months later he was transferred to another Veterans Administration hospital, where a second course of electric shock treatments was administered with curare. After the first curarization, he exhibited a severe, panic-like reaction immediately before each administration of curare. He would sweat profusely, act extremely irritable and tremble violently. His facial expression was that of extreme agitation and fear. At the end of this therapeutic course there not only had been no improvement but there was actually an intensification of his paranoid schizophrenic behavior.

From early childhood this patient was exposed to threatening, rejecting and punishing parents and siblings. His first reactions of defense were shyness and timidity. Parents and siblings consistently

humiliated or threatened him when he turned to them for love and reassurance. Such thwarting of his love impulses led to a retreat to or fixation at a narcissistic level. Since all members of the family exhibited serious personality distortions, his development could not be based on healthy identifications.

In addition, the general emotional pattern of the family revolved about the issues of domination and submission, with no leaven of warmth or affection. Consequently, his general orientation to interpersonal relationships has been in terms of achieving control and avoiding domination. His ordinal position in the family emphasized the necessity of defending himself against being overwhelmed.

His psychosexual behavior has reflected his defenses against being overwhelmed and injured. Both homosexual and heterosexual activities have been viewed as threatening and humiliating rather than as expressions of love. Much of his behavior might represent reaction to considerable castration anxiety.

His marriage to a girl with her own problems of sexual guilt and anxiety for a time was not too threatening to the patient and may have been a defense against homosexual temptations. His homosexual impulses, which would render him passive and defenseless against attack by other men, were mobilized at separation from his wife, when he was alerted for overseas duty. His subsequent paranoid delusions were defenses against this homosexual threat. He probably felt that the birth of his son was a rejection by his wife, so that more narcissistic regression resulted and led to severe hypochondriacal delusion formation. His behavior pattern in the hospital indicated an attitude of defense against possible attack. With this psychologic bias, a procedure such as curarization and electric shock therapy could easily mean to this patient the actual dreaded event, i. e., being rendered completely powerless to resist the attack symbolized by the electric shock. His panic reaction to curarization led to more intense, schizophrenic withdrawal and regressed behavior as defenses against panic.

COMMENT

Brody[3] briefly mentioned that during curarization in modified electric shock therapy "the sense of weakness and choking that follows curare is alarming and causes some patients to refuse to continue the treatment." It is conceivable that this respiratory distress during curarization may represent the ultimate of panic for certain patients in whom psychoses are essentially defenses against a world viewed as threatening to one's very life. Further, the experience of being rendered

3. Brody, M.: Modifications of the Electro-Shock Convulsion by Sodium Pentothal and Curare, J. Nerv. & Ment. Dis. **102**:357 (Oct.) 1945.

incapable of any protective motor act might also precipitate panic in a patient whose psychotic symptoms are defenses against attack, homosexual, castrative or of a less defined type; more intense psychotic mechanisms would then be invoked to protect the patient from his panic feelings.

Such a sequence of behavioral events, in which the treatment maneuver itself becomes the instigating force for further psychotic behavior, must constitute a psychologic complication to the treatment. In the present case it is felt that this sequence occurred and that a psychologic complication to electric shock therapy modified by curare was observed.

Proceeding one step, it is logical to conclude that in the presence of psychotic symptoms raised against fears of being overwhelmed, curare should be administered with serious hesitation, as should any other therapeutic maneuver (thiopental sodium [pentothal sodium®] or unmodified electric shock treatment) which overwhelms the patient physiologically.

From a broader view, this case report has been presented in the hope of focusing attention on the general problem of psychologic complications and contraindications to electric shock therapy. It would seem consistent that the psychosomatic attitude espoused and advanced by psychiatrists should be applied rigorously to the physical treatment methods currently in vogue in psychiatric practice. The injunction of Millet and Mosse [4] that "it is the duty and opportunity of the psychotherapist to investigate the attitude of each patient to the fullest possible extent before proceeding with the [electric shock] treatments," if followed carefully, might lead to pertinent data on psychologic contraindications to shock, as well as possible explanations of the differences in therapeutic benefit obtained in the various psychotic groups.[4]

Investigations in the area of the psychologic consequences of shock quite reasonably can be expected to lead to further refinements in the application of this type of therapy.

SUMMARY AND CONCLUSIONS

The case of a paranoid schizophrenic patient is reported in which panic was exhibited during each administration of curare prior to twenty electric shocks. The psychotic symptoms were more profound at the end of this course of electric shock therapy and curare.

The increase in psychotic symptoms is interpreted as a possible psychologic complication of electric shock treatment modified by curar-

4. Millet, J. A. P., and Mosse, E. P.: On Certain Psychological Aspects of Electro-Shock Therapy, Psychosom. Med. **6**:226 (July) 1944.

ization in a patient whose psychosis represented a defense against physical and sexual threats.

It is proposed that the dynamic mechanism of psychotic symptoms as defenses against attack be considered as a possible psychologic contraindication to the curare modification of electric shock therapy.

It is recommended that further psychodynamic studies of reactions to electric shock therapy and its modifications be made in order to define the psychologic complications and contraindications. Such studies may provide refinements in the administration and understanding of electric shock therapy and other physical treatment technics used in psychiatric practice.

ELECTROENCEPHALOGRAPHIC STUDIES IN SPINAL CORD DISEASE

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ALTHOUGH the applicability of clinical electroencephalography in intracranial lesions has been broadened by the recognition of certain rather characteristic abnormalities produced by subcortical lesions, the influence of primary spinal cord disease on the electroencephalogram has not been clearly defined. It is the prevailing opinion that spinal cord dysfunction, caused by local vascular, compressive or degenerative processes, is not reflected in the brain wave pattern. That this view may not be correct will be brought out by the results of the present study.

There is little or no information in the literature concerning the experimental or clinical relation between the electroencephalogram and pathologic processes in the spinal cord. On the other hand, studies of the effect on electrocortical activity of changes in other portions of the nervous system are in abundance. Adrian, Dusser de Barenne, McCulloch and others [1] have outlined the somatosensory boundaries of the cerebral cortex by the electroencephalographic response to afferent peripheral stimuli. These somatic receiving areas of the cortex are, for the most part, contralateral to the side of stimulation, corresponding to the anatomic sensory thalamocortical pathway. In Adrian's work with ungulates, however, there was an ipsilateral representation of the lips, especially in the sheep and goat, resulting perhaps from the dominance of the smell function (ipsilaterally received in the cortex) in the feeding

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1. Adrian, E. D.: Afferent Areas in Brain of Ungulates, Brain **66**:89-103 (June) 1943. Bremer, F.: Effects of Complete Section of the Afferent Cortical System on the EEG, Compt. rend. Soc. de biol. **127**:355-359, 1938. Dusser de Barenne, J. G., and McCulloch, W. S.: Direct Functional Interrelation of Sensory Cortex and Optic Thalamus, J. Neurol. **1**:176-186 (March) 1938.

habits of these animals. Dempsey, Morison and Morison [2] studied the electroencephalographic response to stimulation of the sciatic nerve in anesthetized cats. Three types of response were found: a primary one with a latency of eight to ten milliseconds, localized in the leg area of the sensorimotor cortex (contralateral greater than ipsilateral); a secondary response with a latency of thirty to eighty milliseconds obtainable from any cortical area; and, lastly, an inhibition of spontaneous cortical activity. The afferent pathways for each of these responses were found to be: lemniscal-thalamic for the primary response; both crossed and uncrossed paths for the second response, and paths through the midline structures of the midbrain for the period of inhibition.

Other studies have included descriptions of the brain potential records associated with voluntary [3] and involuntary muscle activity. Girden [4] has shown that the induction of complete striated muscle paralysis in the dog, using a peripheral poison such as erythroidine, does not affect the normal cortical activity so long as proper artificial respiration is maintained. In no recorded investigation has there been a study of the effect of experimentally produced direct spinal cord lesions on the electroencephalogram.

In a recent report, Pacella and Jungeblut [5] described the electroencephalographic changes in monkeys and guinea pigs with experimentally induced poliomyelitis and in a group of 17 human patients convalescent from poliomyelitis. In monkeys, no changes were observed before the onset of fever or paralysis after intracerebral inoculation, but abnormalities appeared and became more conspicuous during the paralytic stage. Of the series of convalescent patients examined, all of whom had residual paralyses, only 2 exhibited definitely abnormal electroencephalographic patterns. Because these 2 patients had been maintained in the respirator for some time, Pacella and Jungeblut expressed the belief that a diagnosis of polioencephalitis was quite probable, explained the abnormalities of electrocortical activity on that basis and stated that "since classic poliomyelitis is essentially an infection with localization in the anterior horn of the spinal cord, the absence of electroencephalographic changes . . . is not surprising."

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2. Dempsey, E. W., and Morison, R. S.: Production of Rhythmically Recurrent Cortical Potentials after Localized Thalamic Stimulation, Am. J. Physiol. **135**:293-300 (Jan.) 1942.

3. Jasper, H. H., and Andrews, H. L.: Brain Potentials and Voluntary Muscle Activity in Man, J. Neurophysiol. **1**:87-100 (March) 1938.

4. Girden, E.: Effect of Striated Muscle Paralysis Induced with Erythroidine upon Electroencephalogram, Proc. Soc. Exper. Biol. & Med. **53**:163-164 (June) 1943.

5. Pacella, B. L., and Jungeblut, C. W.: The Electroencephalogram in Poliomyelitis, Arch. Neurol. & Psychiat. **58**:447-451 (Oct.) 1947.

Our interest in the possible reflection of spinal cord disease in the electroencephalogram was first aroused during the diagnostic study of 2 patients with partial paraplegias. Although defined sensory levels were lacking in these cases, pathologic change in the spinal cord was suspected and later confirmed. Routine electroencephalograms revealed identical abnormalities, simulating the abnormalities often encountered with parasagittal intracranial lesions. With this confusing circumstance of a partial paraplegia conforming clinically to spinal cord disease but with electroencephalographic changes consistent with an intracranial pathologic state, it became necessary to resolve this diagnostic difficulty by an electroencephalographic investigation of a series of patients with proved pathologic alterations of the spinal cord. This report presents the preliminary results of this study.

CLINICAL MATERIAL

Fifteen patients with clinical and laboratory evidence of spinal cord disease were chosen for electroencephalographic study in consecutive order from the

TABLE 1.—*Types of Lesions*

Diagnoses	No. of Cases	
	Total	No. Surgically Proved
Exostoses of vertebral column and/or arachnoiditis	6	4
Tumors compressing cord (myeloma, sarcoma, meningioma, epidural granuloma, glioma)	5	5
Thrombosis, anterior spinal artery	1	1
Syringomyelia	1	0
Abortive Friedreich's disease	1	0
Undiagnosed level lesion (T6)	1	0
Total	15	10

Bellevue Hospital neurologic service. The series included 9 men and 6 women. Their ages varied from 17 to 73, with every decade represented. Among the entire group, there was no personal or family history of epilepsy or related disorders. One of the women had a history of several mental depressions; the last terminated seven years before admission. All but 2 of the patients described slowly progressive paraplegias of varying durations. Of the 2 with a different type of onset, 1 had a sudden spontaneous paraplegia and the other a sudden partial conus and cauda equina traumatic lesion nineteen years before admission. None of the patients was taking any specific drugs during the study.

The lesion of the spinal cord was visualized and proved surgically in 10 of the 15 patients. Of the other 5 patients, 4 had rather typical clinical indications of spinal cord disease. The remaining 1 presented an unproved diagnostic problem, many of the signs and symptoms pointing to a lesion of the cervical portion of the cord. Studies for an intracranial lesion, including air encephalography, gave negative results, but the electroencephalogram contained abnormalities similar to the others in the series. The types of lesions encountered are listed in table 1.

A Grass six-channel apparatus was employed. Standard electroencephalographic technic was used with "bipolar" recordings as well as the so-called "unipolar" (with ear electrodes as reference leads) recordings. All the patients had frontal,

TABLE 2.—*Summary of Clinical Data*

Case	Age	Sex	Diagnosis	Duration, Yr.	Level	Side	Pain	Progression	Motor Changes	Adventitious Movements	Sensory Changes	Blood Sugar, Mg./100/Cc.	Hgb., Gm.	RBC, Millions	CSF Block	Operation
1	32	M	Herniated intervertebral disk	1	C5-6	L	—	Slow	Spastic paraparesis	Fasciculations, right deltoid	None	80	15	5.0	None	—
2	40	M	Abortive Friedreich's ataxia	11	Dorsal	R	—	Slow	Spastic paraparesis	.....	Impaired position sense	87	17	5.5	None	—
3	64	M	Arthritic exostosis	8	C6	Motor on R; sensory on L	+	Slow	Spastic paraplegia with hand atrophy	Fibrillations, both hands	Vague, severer on L.	80	16	5.0	Intermittent	+
4	48	M	Herniated disk and exostosis	9	C5	R	±	Slow	Spastic paraplegia with hand atrophy, R.>L.	Fibrillations both deltoids	Inconstant	85	14	4.7	None	+
5	26	F	Epidural granuloma	5/52	C7-8	Both	—	Rapid	Flaccid paraplegia	.....	Level at C8	83	12	4.2	Complete	+
6	39	F	Thrombosis of anterior spinal artery	¼	D7	Both	—	Stationary	Flaccid paraplegia	.....	Level at D7, sparing vibration and position sense	84	10	4.2	None	+
7	54	M	Solitary plasma cell myeloma	5	D2-4	R	—	Improving	Spastic paraparesis	.....	None	77.	13	4.2	Partial	+
8	62	M	Old fracture-dislocation of spine	19	D12-L1	R	—	Stationary	Right foot drop	Fibrillations, right gluteals	None	71	15	5.2	Partial	—
9	55	F	Constrictive arachnoiditis and meningioma	8	C7-D3	R	—	Slow	Spastic paraplegia	.....	Absent vibration and position sense	74	14	4.5	Complete	+
10	17	F	Ewing's sarcoma of lumbar spine	¾	Cauda equina	Both	—	Stationary	Flaccid paraplegia	.....	Impaired below L3	85	14	4.8	Not done	+
11	38	F	Intramedullary cord tumor	⅔	C6-8	Both	+	Slow	Spastic paraplegia	Flexor spasms	Impaired below C8	64	13.8	4.1	Partial	+
12	37	M	Vascular cord lesion	3	D6	Both	—	Stationary	Spastic paraplegia	Flexor spasms	Absent below D6	85	14	4.5	None	—
13	59	F	Arachnoiditis	1¹/₁₂	C5	Motor on R	+	Slow	Right spastic hemiparesis	.....	Impaired on L below C7	88	15	5.0	Intermittent	+
14	49	M	Syringomyelia	4	C5	Sensory on L	—	Stationary	No weakness	.....	Impaired on L below D5	89	14	4.8	None	—
15	73	M	Arthritic exostosis	1	C5	Both	—	Slow	Spastic paraplegia	Fibrillations, both deltoids	Inconstant	84	13	4.0	Intermittent	+

central, postparietal, occipital, temporal, vertex and precentral sagittal leads. Some had bilaterally placed precentral leads as well.

Table 2 summarizes the pertinent clinical data in the 15 cases in the series. The corresponding electroencephalographic abnormalities are listed in table 3.

COMMENT

The striking feature of this study is the fact that not a single one of the patients had a normal electroencephalogram. The specific

TABLE 3.—*Electroencephalographic Abnormalities*

Case	Paroxysmal Quality*	Mode of Occurrence and Background Activity	Spiking†	Lateralization	Localization‡
1	M	Intermittent; fluctuating choppy background	±	Left	C, S, PC
2	M	Intermittent; alpha pattern chiefly posteriorly	±	Left (occ. to right)	C, T, S
3	M	Intermittent; alpha pattern chiefly posteriorly	+	Shifts	C, PC
4	M	Intermittent; diffuse alpha background	—	Shifts	C to V
5	M	Intermittent; diffuse alpha background	—	Shifts	C
6	M	Intermittent; fluctuating alpha pattern	+	Left	C, PC, PP, T
7	V	Continuously abnormal; some alpha posteriorly	+	Fast on left Slow on right	C, PC
8	S	Slightly intermittent; disorganized alpha	—	No difference	Diffuse
9	V	Continuously abnormal	—	Left (asymmetric)	C, S, PP
10	V	Frequently recurrent; some alpha, chiefly posteriorly	—	No difference	C, S
11	V	Intermittent; fluctuating background	+	Shifts	C, S
12	M	Infrequently intermittent; diffuse alpha background	±	No difference	Diffuse
13	S	Infrequently intermittent; predominant alpha	+	No difference	Frontal
14	M	All continuously abnormal	—	Left	PP (irregular slowing) C (very fast, bilaterally)
15	M	Frequently recurrent; good alpha background	±	Left	C

* S = slightly paroxysmal; M = moderately paroxysmal; V = very paroxysmal.
† + = marked spiking; — = no spiking; ± = occasional small spikes.
‡ Localization: C = central (motor); PC = precentral; PP = postparietal; T = temporal; S = sagittal; V = vertex (between C and PP).

abnormalities varied somewhat but may be classified descriptively into five groups of records: 1. Disorganzied alpha activity with fast and slow activity slightly beyond the limits of normal (case 8). 2. Intermittent runs or bursts of moderately slow and slightly fast activity, including short spikes, against a background of fluctuating amplitude and pattern (cases 1, 2, 3 and 14). In case 14 there was very fast activity in the motor regions with irregular slowing, nonparoxysmal, in the parieto-occipital regions. 3. Predominant, rather than intermit-

tent or paroxysmal, moderately slow activity interspersed with fast potentials (cases 9 and 10). In 1 of these 2 cases (case 10) there were in addition, runs of irregular 3 per second waves superimposed on the fast activity and augmented by hyperventilation. 4. Well organized

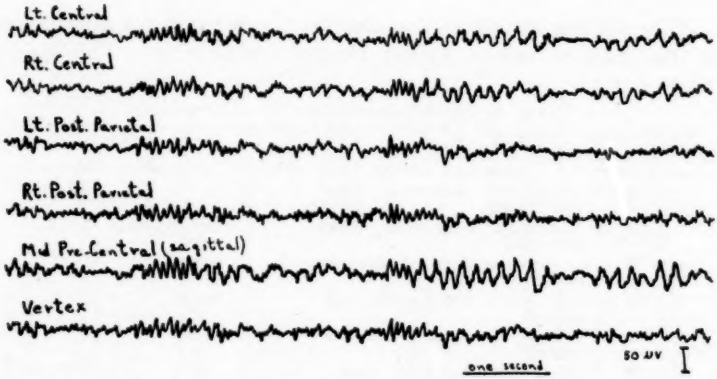

Fig. 1 (case 1).—A pattern of fluctuating activity, consisting notably of 12 to 13 per second activity, low voltage fast potentials and moderate voltage 6 to 6½ per second waves, the latter being most evident in the central and sagittal central regions.

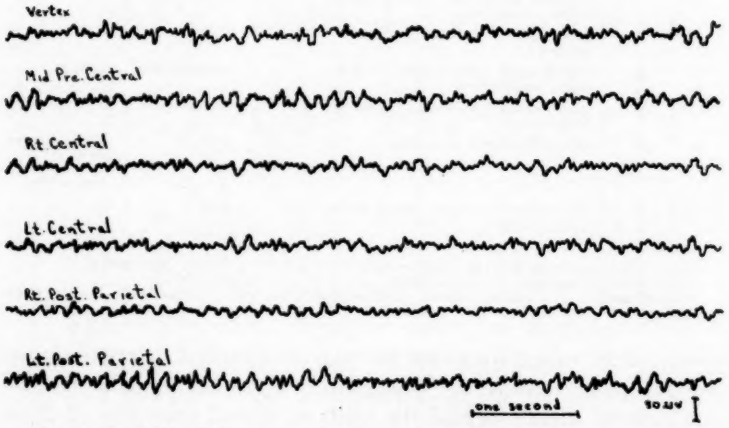

Fig. 2 (case 9).—Diffusely, moderately slow pattern of activity with superimposed low voltage fast potentials and some bilateral asymmetry in amplitude.

alpha patterns but containing higher and slightly slower runs or single high waves centrally (cases 4, 5, 6, 12, 13 and 15). In one of these cases (case 6), more severely abnormal than the others, there were

sharp wave forms or single high voltage spikes. In another (case 13) the slower runs appeared frontally rather than centrally. 5. Exceedingly abnormal records, characterized by high voltage fast (24 to 30 per second) activity, spikes and bursts of high (8 to 12 per second) or slower activity and at times containing a spike component (cases 7 and 11).

The quality, not the severity, of these records is what is most striking. The paroxysmal features run between two extremes, from the recurrent brief appearance of borderline abnormal frequencies occurring in a voltage slightly higher than that of the background activity to the full-blown paroxysmal discharges. A classification of the fifteen records, based on this paroxysmal quality, is offered in table 4.

The range of the slow frequencies fell chiefly between 5 and 7 cycles per second, several showing 6 or 6 to 8 per second activity. Paroxysmal bursts occurring in relatively high amplitude varied within the range

TABLE 4.—*Classification by Paroxysmal Quality*

A. Slightly paroxysmal (infrequent slightly fast or slow activity occurring against a background of relatively normal activity) (cases 8, 13)	2
B. Moderately paroxysmal (intermittent slow and/or fast activity, constituting either the predominant feature of record or recurring frequently against a background of normal activity) (cases 1, 2, 3, 4, 5, 6, 12, 14, 15)	9
C. Very paroxysmal (burst of high fast or high slow, and spikes or spike-wave formations) (cases 7, 9, 10, 11)	4

of 8 to 12 per second. In 9 of the 15 cases, the paroxysmal, moderately slow activity was increased during and/or after hyperventilation. (In 1 of these 9 records, most of the abnormality appeared after hyperventilation.) In 3 of the 15 cases, hyperventilation was performed poorly and was unaccompanied with significant alterations. In 1 of the 15 (case 14), there was increase in focal irregular slowing. In 1 other case (case 4), there was no perceptible change after hyperventilation; and in the last of the 15 (case 6), there was a slight increase in the amplitude and paroxysmal quality of the record.

The localization of the abnormal electroencephalographic features was conspicuous, the central, sagittal central, precentral and sagittal precentral regions showing the greatest involvement. The vertex and postparietal regions were much less conspicuously involved, although in several cases the activity from the central regions was reflected slightly more posteriorly than rostrally. In several records, the derivations from the temporoparietal regions were also involved. This abnormality was not entirely unlike that reported by Walter and Dovey [6] in a

6. Walter, W. G., and Dovey, V. J.: Electroencephalography in Cases of Subcortical Tumor, J. Neurol., Neurosurg. & Psychiat. **7**:57-65 (July-Oct.) 1944.

study of subcortical tumors. They described such activity in the 4 to 7 per second band, usually bilateral and most prominent in the parietotemporal areas, as the "theta" rhythm and suggested that such rhythms are characteristic of the isolated parietotemporal cortex. In

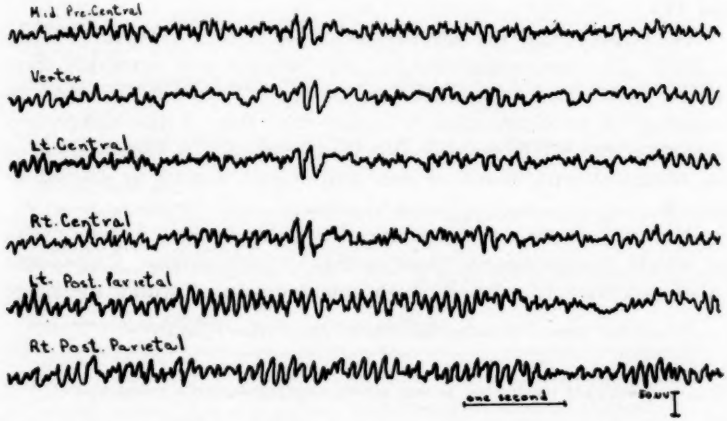

Fig. 3 (case 5).—A predominant, well organized 9 to 10 per second pattern interrupted at infrequent intervals by single, higher and slightly slower waves in the central regions.

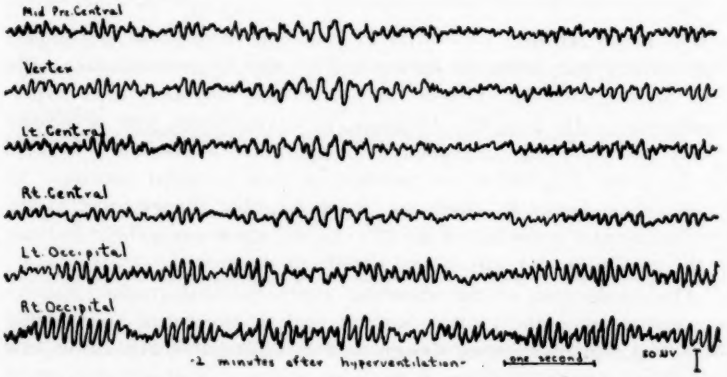

Fig. 4 (case 5).—Recurrent runs and bursts of 5 to 7 per second waves appearing for three minutes following hyperventilation and varying from moderate to high voltage.

1 case, the slower activity appeared frontally and was increased during and after hyperventilation. Bilateral differences in the electroenceph-

alogram were a conspicuous feature, with the abnormal features either remaining consistently greater in one hemisphere than the other or shifting in prominence from one hemisphere to the other.

Tables 2 and 3, summaries of the pertinent clinical and electroencephalographic data for the series, list the factors which might later

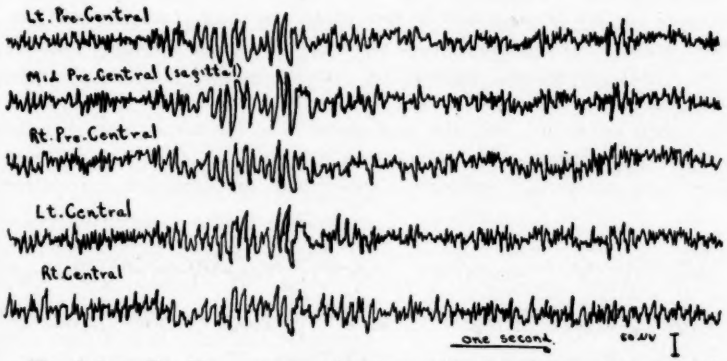

Fig. 5 (case 7).—Very paroxysmal pattern, with abnormality most marked in the central and precentral regions; this strip demonstrates the prevalence of fast potentials intermittent with bursts of very high alpha rate activity, occurring above at a rate of 11 to 12 cycles per second.

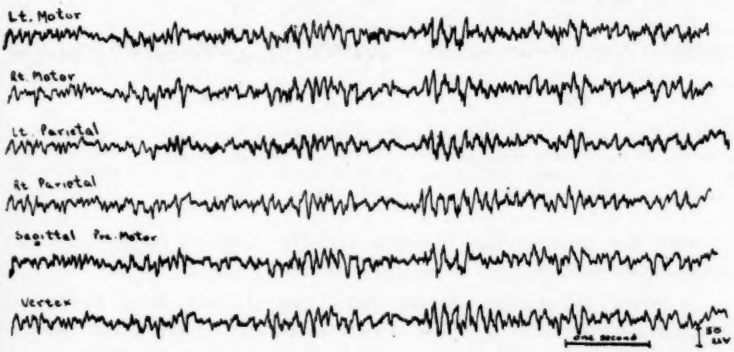

Fig. 6 (case 11).—Recurrent runs of 5 to 7 per second waves occurring against a background of low voltage fast potentials, intermittent alpha activity and brief bursts of 16 to 22 per second waves.

be used in supplying meaningful information about the results. No such correlation of data will be made in this preliminary report because of the number of variables and the small size of the series.

Little comment has been made concerning the mechanism by which spinal cord lesions might produce abnormal electrocortical activity. The

only recent experimental work which influences this consideration is that by Woolsey and Chang [7] on antidromic volleys from the medullary pyramid. They defined the cortical origin of fibers traversing the medullary pyramid in the rabbit, cat and monkey by stimulating the pyramid electrically and recording oscillographically the cortical responses set up by the antidromic volleys. These responses were initially surface positive and in the cat and monkey consisted of a fast brief wave, corresponding to a conduction velocity of approximately 100 meters per second, followed by a more complex slow wave. The amplitudes of these two types of waves varied with the species, the rabbit exhibiting only the slow wave. On the assumption that the form of the response is determined by activity in fibers of different sizes and conduction velocities, there was an apparent correlation

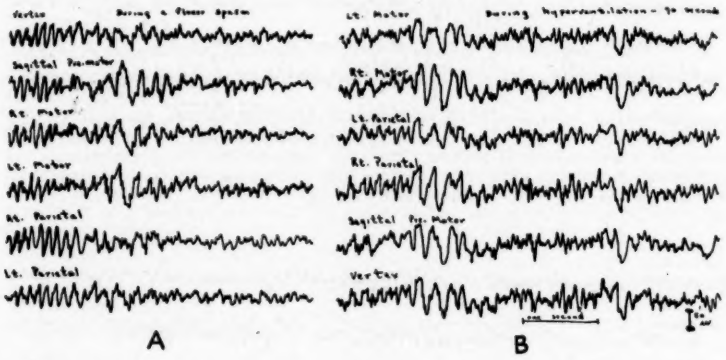

Fig. 7 (case 11).—*A*, a burst of high voltage 3 to 4 per second discharges, most marked in the motor and premotor regions, occurring during a flexor spasm. *B*, exacerbation of these high, slow discharges occurring during (and after) hyperventilation.

between the form of the response and the fiber constituents of the pyramids as described for these three species by Lassek.[8]

Woolsey and Chang demonstrated that the region of cortex in which the antidromic response occurs is similar in the three species, including Brodmann's areas 6, 4, 3, 1, 2, 5 and 7 in the monkey and the homologous areas in the cat and rabbit. In the monkey both components of the response were best developed in area 4, but they were almost as large in the postcentral gyrus. In the cat, responses were

7. Woolsey, C. N., and Chang, H. T.: Cortical Origin of the Pyramidal Tract as Defined by Antidromic Volleys from the Medullary Pyramid, Federation Proc. **6**:1 (March) 1947.

8. Lassek, A. M.: Human Pyramidal Tract: Critical Review of Its Origin, J. Nerv. & Ment. Dis. **99**:22-28 (Jan.) 1944.

greatest in the Betz cell area. Afferent responses were avoided by stimulating at a frequency too rapid for thalamic transmission.

With this work as a background, it is conceivable that slowly progressive spinal cord lesions set up electrochemical changes which result in the production of such antidromic impulses in the pyramidal tracts, a cord pathway which, perhaps, is the most vulnerable to noxious influences. This not only would explain the occurrence of abnormal electroencephalograms in these cases but would account for the special localization of these abnormalties in the vast majority of cases.

SUMMARY

Electroencephalographic abnormalities in 15 patients with spinal cord disease, without a personal or family history of epilepsy, are described in this preliminary report.

The striking feature of these abnormalities, which in most of the cases were moderate in degree, was the paroxysmal quality of the records and the frequent localization of these abnormalities to the central, sagittal and precentral regions.

Although these abnormalities are not easily explained, recent work suggests that antidromic volleys in the pyramidal tracts may be a factor.

Recognition of these abnormal electroencephalograms is important clinically in distinguishing between spinal cord disease and parasagittal intracranial lesions in the causation of ill defined partial paraplegias.

MUSCULAR ATROPHY AND PSEUDOLOGIA FANTASTICA ASSOCIATED WITH ISLET CELL ADENOMA OF THE PANCREAS

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A CASE is reported in which prolonged hypoglycemia due to an islet cell tumor of the pancreas was accompanied with an unusual array of symptoms due to widespread damage of the central nervous system. The patient had had repeated convulsions, periods of confusion and excitement, ataxia, muscular atrophy, intellectual impairment and pseudologia fantastica. After removal of the pancreatic adenoma, all abnormalities except the muscular atrophy disappeared. It has been recognized that deprivation of glucose essential for metabolism of the nerve cells can cause irreversible damage of the brain and spinal cord, but involvement of the central nervous system as extensive as in the present case has rarely been reported. Both the relationship of a syndrome resembling progressive muscular atrophy to spontaneous hypoglycemia and the recovery of a patient with pseudologia fantastica seem of unusual interest.

REPORT OF A CASE

The patient, a 23 year old veteran, came to our attention after he had been readmitted to the Veterans Administration Hospital at Fort Howard, Md., in

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From the Veterans Administration Hospitals, Fort Howard, Md., and Perry Point, Md.

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June 1946. He complained of severe difficulty in walking and talking, which had fluctuated but gradually increased in severity over a period of two years. The patient said that he had been unconscious for several days following an airplane crash in 1944 and had been unable to move or speak for some days after gaining consciousness. However, the entire history obtained from the patient was found to be fallacious, and it was necessary to reconstruct the story from information gained from relatives and Army records. He had first suffered an attack of unconsciousness in 1942 while working in a shipyard prior to induction. There may have been several attacks of sudden weakness of the legs during the same period. The difficulties were considered trivial and did not lead to medical study. He was first hospitalized in June 1944, while serving in the Air Forces, because of a spell of unconsciousness. The examinations were unrevealing, and he was returned to duty. In September 1944 he was hospitalized because of convulsions. During the next month and a half he suffered numerous seizures and occasional attacks of acute excitement. Several weeks after admission scanning speech and ataxic gait were noted. A glucose tolerance test showed a low blood sugar level on each determination. He was discharged from the Army with the diagnosis of spontaneous hypoglycemia, cause undetermined.

The convulsive seizures continued after discharge, and his relatives noted a profound alteration in his personality. He was admitted to the Veterans Administration Hospital at Fort Howard in January 1945 but left against advice before studies could be started. When he was readmitted in June 1945, the fabricated account of his life and illness was sufficiently plausible to be accepted and it completely misled the examining physicians. Physical examination revealed a waddling gait, a bizarre speech disorder which fluctuated in severity and incoordination of hand movements. Various laboratory tests, including examination of the spinal fluid, were unrevealing aside from the glucose tolerance curve. After ingestion of 100 Gm. of glucose the blood sugar rose slowly from a fasting level of 51 mg. to reach 83 mg. per hundred cubic centimeters after two hours. During the hospital stay he suffered one mild epileptiform seizure and on another occasion was combative, resistive and irrational for several hours. He was finally discharged in August 1945 without definite diagnosis. It was considered that he suffered from major hysteria. His disorders gradually increased in severity. He became unable to climb stairs because of foot drop; speech became more inarticulate, all movements clumsier and his behavior increasingly irresponsible.

There was no history of pertinent hereditary disease; the family was certain that there had been no epilepsy or dystrophic or cerebellar disease in either line. The mother had died of cancer at an early age. The father, two brothers and two sisters were living and well.

The patient had been in good health until the onset of his present illness. He had lived in an orphanage between the ages of 6 and 17. One brother had been adopted by an aunt and uncle in infancy, and the other siblings had been placed in foster homes. The patient had completed high school while in the orphanage and had then lived with his aunt and uncle in Baltimore. He never fitted into the family and was clearly jealous of his cousins and his brother. He worked regularly in a shipyard, earning as much as $100 a week, but had as little to do with his relatives as possible. His uncle had no complaints about his behavior prior to induction but believed that he had spent money too freely attempting to impress girls and disliked the attitude of superiority adopted by the patient. He had joined the Air Forces against the wishes of his family and completed preaviation cadet training. Sent to gunnery school, he was grounded because of "shaking spells and nervousness." He had never been overseas. His character

seemed to have changed after his discharge from the Army. He spent most of his time pretending to be very wealthy. He altered his discharge papers and claimed to have received many decorations for combat duty. He maintained that he had studied engineering at the university at which he had received Army training. He became unreasonable and antagonistic toward his relatives and insisted on living in a rooming house.

At the time of his readmission to the hospital, in May 1946, the true history remained unknown. The story given by the patient adhered to that given on the previous admission but had been further elaborated. The emphasis was placed on the onset of his illness following an airplane crash in which nine persons had been killed.

Physical Examination.—The pertinent observations were limited to the neurologic. There was a gross disturbance of gait. The patient waddled like a dystrophic child, and ataxia added a lurching quality. The difficulty in analyzing the disorder of locomotion was enhanced by steppage gait due to bilateral foot drop. There was difficulty in standing erect even with the eyes open, as he swayed and then lurched, but not in any given direction. Speech was badly garbled, with a scanning quality. The small muscles of the hand were symmetrically wasted; flexion and extension of the wrist were very weak, and abduction and adduction of the fingers were absent. The muscles of the upper arm were moderately strong.

TABLE 1.—*Fasting Blood Sugar Levels Immediately Before and After Removal of Pancreatic Adenoma*

	Pre-operative Level, Mg./100 Cc.	Postoperative Level, Mg./100 Cc.			
		2 Days	3 Days	5 Days	7 Days
Fasting blood sugar.....	54	156	153	137	95

The truncal musculature was weak, and the patient could raise himself from the supine position only by climbing up on himself. The muscles of the calves were small and weak. Plantar flexion of the foot was very weak and dorsiflexion impossible. No fibrillations were noted anywhere. There was marked dysmetria of movements of the upper extremities. In pointing rapidly he constantly overshot the mark. Rapid tapping and rotatory movements were carried out very poorly. There was no lateral past pointing. Rebound was not abnormal. Deep reflexes were present and equal in the upper extremity but difficult to elicit. Knee jerks were weakly present, but the ankle jerks were absent. No abnormal reflexes were found. Sensation to light touch, pinprick, vibration, deep pain and muscle-joint position sense were everywhere intact. The cranial nerves were normal aside from the suggestion of sagging of the facial musculature and the labored movements of the lips and tongue.

The results of routine laboratory studies were all normal on admission, including examination of the spinal fluid and a fasting blood sugar level of 73 mg. per hundred cubic centimeters. Roentgenograms of the skull, lumbar portion of the spine and chest revealed normal conditions. Subsequent abnormal blood sugar levels are noted in tables 1 and 2. The electroencephalogram gave evidence of diffuse cortical damage.

Behavior and Content.—The patient maintained an attitude of pleasant superiority, requesting and accepting special privileges as if accustomed to them. Although he expressed concern over his condition and desired help, he rarely seemed dejected. He acted as if he were being a good sport rather than euphoric.

His entire life history was confabulated, but, since he offered little spontaneously, the unlikelihood of his story was not recognized upon admission. When it became necessary for him to elaborate on his background, inconsistencies appeared. He claimed that he was the son of a Jewish father and a gentile mother, a member of a prominent wealthy family. He had been reared by a wealthy maternal aunt. He had completed high school at the age of 13½ and gained an engineering degree at the age of 19, when he enlisted in the Air Corps. He was not interested in his pension particularly, as he had an inheritance of a quarter of a million dollars from his mother and owned a chain of dry cleaning stores in Baltimore, which an uncle ran for him. The ability to concoct a story that might fit the facts known to the examiners was illustrated by several sidelights. It was known that the uncle in Baltimore was Jewish and had a different name from that of the patient. He had said that the aunt in Baltimore was his father's sister, whereas in reality the uncle was his mother's brother—an alteration of the facts necessary to explain that the uncle's name was different from his and still permit his mother to be a gentile. When the ownership of the chain of cleaning stores

TABLE 2.—*Results of Glucose Tolerance Tests Before and at Indicated Intervals After Removal of Pancreatic Adenoma*

Hours After 100 Gm. of Glucose	Typical Pre-operative Level, Mg./100 Cc.	Postoperative Levels, Mg./100 Cc.					
		8 Days	11 Days	15 Days	4 Mo.	7 Mo.	1 Yr.
Fasting	54	117	91	105	91	142	111
½	74	...	95	100	...	...	...
1	70	142	105	100	142	181	125
2	97	117	95	103	118	95	100
3	62	...	105	86	111	83	100
4	50	...	91	95	98	83	87
5	..	...	..	...	...	77	105
6	..	...	..	...	...	77	105

was questioned on one occasion, he produced a summons to appear in court for a trial involving the firm, as garments had been stolen. It later turned out that his uncle had owned the stores and the patient had stolen and pawned a number of the garments and had been found out. When confronted with evidence, he shifted his story only to the extent of saying that he was accepting the blame in order to shield his brother who he was quite certain had been involved in the thefts.

The patient's account of his military career, though brief at first, was elaborated when he was questioned. With apparent reluctance, he narrated deeds which would have made him one of the heroes of the Air Corps. The story told to any one person was always consistent, but it soon became apparent that the details told to various persons could not be correlated.

When it became clear that the history was a confabulation, he attempted to defend his statements by various ruses. For example, he claimed that the Army records which had been obtained failed to mention any airplane accident because he had flown without permission and the medical officers were kind enough not to wish to make his injuries "not in the line of duty." At other times, he became angry and simply refused to discuss his statements further. Under this pressure, he became hostile toward the physicians in the hospital and threatened to leave.

During the five months following admission, he suffered from at least one generalized convulsion, which lasted from ten to twenty minutes. No localizing signs were ever noted. The patient also reported that he suffered from episodes of unconsciousness early in the morning, but these were never witnessed. On other occasions, he said that after awakening in the morning he was completely unable to move for some minutes and that sometimes he would crumple in a heap on the flood when he got out of bed. Several times he suddenly became confused and belligerent. His behavoir deteriorated. He became loud and boisterous, upsetting the hospital routine in many ways. He made advances to the nurses and finally struck one without apparent provocation. He grew increasingly uncooperative and refused to undergo various tests which were necessary to find the cause of his hypoglycemia. He was placed on a high carbohydrate diet with intermediate feedings of sugar, but by this time it was difficult to gain any cooperation from him. As he was upsetting the entire ward, refused operation and insisted that he be permitted to leave the hospital, he was committed to the Veterans Hospital, Perry Point, Md., for completion of studies and for operation.

On admission to the hospital at Perry Point, he informed the admitting officer that he had a tumor of the pancreas and required sugar to avoid weak spells. The neurologic findings were unchanged. He was courteous but supercilious, maintaining a euphoric attitude toward his severe disability. The story of his military exploits had been further elaborated. When pressed concerning inconsistencies, he became belligerent, claiming that the source of his income and his family affairs were no concern of the hospital. Finally, when confronted with the Army records, he stated that there were two men of the same name and the records sent by the Army were those of the other man. He was fully oriented, and no memory defects could be noted.

Mental Tests.—On the Weschler-Bellevue Test[1] given on November 6, he attained a verbal intelligence quotient of 114 and a performance intelligence quotient of 80, which was considered indicative of mental deterioration. On the Hartford-Shipley Scale,[2] he attained a vocabulary score of 17 and an abstract score of 12, giving him a conceptual quotient of 71, which also indicated an organic deterioration.

Laboratory Studies.—A wide range of laboratory studies were carried out to make certain that the hypoglycemia was due to hyperinsulinism. Several liver function tests gave results within normal limits. Otherwise, the tests, aside from the blood sugar determination, did not add pertinent information. Fasting blood sugar levels ranged between 37 and 72 mg. per hundred cubic centimeters, and a glucose tolerance test continued through three and one-half hours showed a fasting sugar level of 54 mg., which rose to a high point of 97 mg. between one hour and two and one-half hours and then dropped to 67 mg. in three and one-half hours.

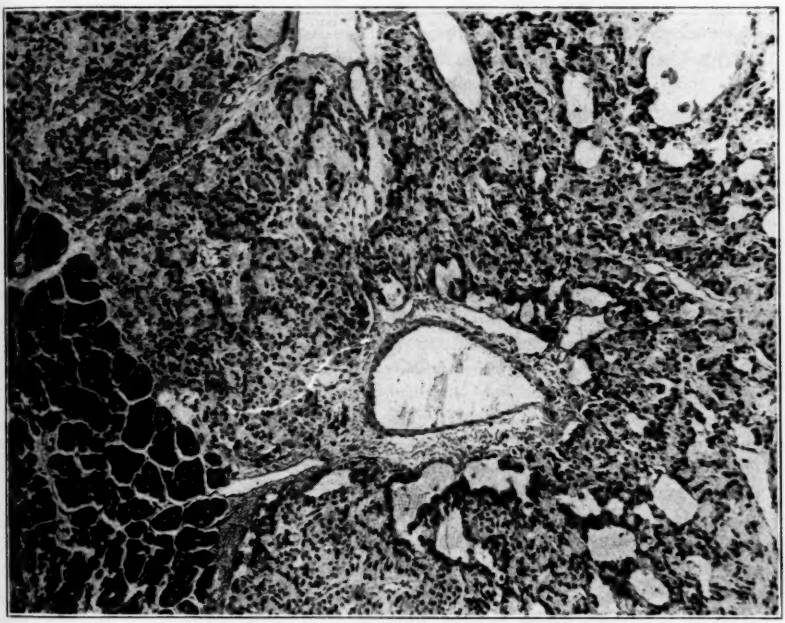
Attacks were partially controlled by a high carbohydrate diet given in frequent feedings. Under psychiatric supervision and the altered diet, his emotional state improved, for, though he continued to voice his fabrications, he became more reasonable. He had become paranoid about the doctors in Fort Howard and insisted that he was going to sue them for false commitment. Despite this, he now

1. Wechsler, D.: The Measurement of Adult Intelligence, Baltimore, Williams & Wilkins Company, 1939.

2. Shipley, W. C.: A Self-Administering Scale for the Measuring of Intellectual Impairment and Deterioration, J. Psychol. **9**:371 (April) 1940.

agreed to have the operation and was perfectly willing to be transferred back to the hospital at Fort Howard, where the facilities for major surgery were, at that time, superior. There was no appreciable change noted on his return to Fort Howard in February 1947, and after completion of some laboratory studies, with results similar to those previously obtained, the pancreas was explored.

Operative Report.—A reddish purple nodule which measured approximately 1.5 cm. in diameter, which was firm and seemed completely encapsulated, was found immediately on the anterior surface of the pancreas. Enucleation of the tumor from the substance of the pancreas was carried out easily. Careful search failed to reveal other tumors.



Low power photomicrograph of section from the adenoma removed from the pancreas. Note the sharp demarcation from normal pancreatic tissue.

Pathologic Report (By Dr. William B. VandeGrift, Pathologist, Veterans Hospital, Fort Howard).—The specimen was a nodule weighing 1.6 Gm., which was almost completely encapsulated, with clearcut demarcation from normal pancreatic tissue. Approximately 80 per cent of the cells contained abundant, vacuolated basophilic cytoplasm and round medium-sized nuclei containing a single nucleolus with chromatin distributed in a fine even network. These were identified by special stains as "beta cells." The remaining cells were eosinophilic cytoplasm and were identified as "alpha cells," which are similar to those seen in the normal islands of Langerhans, although the nucleoli were less distinct.

Postoperative Course.—The immediate postoperative course was uneventful. The fasting blood sugar level rose immediately, and the glucose tolerance curve

gradually returned to normal (tables 1 and 2). There have been no convulsions or episodes of sudden weakness in the ensuing fifteen months. The patient was readmitted for follow-up studies in June and September 1947 and March 1948. A gradual but striking change in his neurologic and mental status occurred. Three months after the operation the ataxic component of his motor disorder had disappeared, and there was some suggestion of increased strength in his finger and arm movements. Subsequently there was clearcut improvement in his speech, which had been deteriorating rapidly prior to operation, and definite gain in strength of ability to abduct and adduct his fingers against resistance. Gait improved, but it was considered that the improvement might be due to loss of the ataxia and to practice. While it is difficult to state that there was improvement in his muscular strength, it is certain that there was no progression of the muscular atrophy following the removal of the tumor.

The changes in the intellectual and emotional spheres were even more marked. Soon after the operation the patient recognized that his behavior had been irrational. The confabulated account of his life disappeared, and he offered a history of his life that was factual, though he remained mixed up about events after the onset of his illness. He began to make provisions for his future on a realistic basis and studied to prepare for college. At first he was slightly euphoric, but finally his mood became appropriate to concurrent situations. At first his judgment seemed impaired, for, despite his friendliness toward the physicians, he adhered to his former determination to sue the same physicians because of illegal commitment. A year after the operation he expressed his gratitude for the interest of the physicians and spoke freely of "how crazy" he must have been to threaten suit. At the same time he recognized that his limitations made an engineering education unfeasible and decided to accept a position in his uncle's business. The unreasonable hostility toward his relatives had completely disappeared, and he now willingly accepted the help they had always proffered.

Improvement in intellectual functioning paralleled the improvement in behavior and emotional responsiveness. In June 1947, although no clearcut difficulty in memory functions could be found,[3] he achieved a mental age of only 13 years 10 months on the Kohs Block Test as compared with a mental age of 15 years 3 months on the vocabulary test.[4] Although the discrepancy between the performance on the two tests is not diagnostic of intellectual impairment, the impression was substantiated when in September he achieved a mental age of over 17 years on the Kohs Test.

COMMENTS ON THE SYMPTOMATOLOGY

The numerous neuropathologic reports of severe damage to the brain following severe and prolonged hypoglycemia have been reviewed and collated by Lawrence, Meyer and Nevin.[5] Widespread damage both with and without hemorrhage have been found. Characteristic observations are diffuse degeneration and necrosis of nerve cells with

3. Lidz, T.: The Amnestic Syndrome, Arch. Neurol. & Psychiat. **47**:588 (April) 1942.

4. Lidz, T.; Gay, J. R., and Tietze, C.: Intelligence in Cerebral Deficit States and Schizophrenia, Measured by Kohs Block Test, Arch. Neurol. & Psychiat. **48**:568 (Oct.) 1942.

5. Lawrence, R. D.; Meyer, A., and Nevin, S.: The Pathological Changes in the Brain in Fatal Hypoglycemia, Quart. J. Med. **11**:181 (Oct.) 1942.

corresponding glial proliferation. In the six brains examined by Lawrence and colleagues,[5] the cerebral cortex, the caudate nucleus and the putamen were most affected, the cerebellum less so, and the lesions in the remaining centers of the brain stem were slight. Moersch and Kernohan [6] appear to have published the only report of changes in the spinal cord.

A case reported without neuropathologic study by Blau, Reider and Bender [7] bears the closest resemblance to the present case. The patient suffered from convulsions, parkinsonism, pyramidal signs, ataxia, generalized muscular weakness with myotatic irritability and sensory changes and from progressive emotional and intellectual deterioration accompanied by paranoid delusions. Fibrillations were noted in the forearm during hypoglycemic attacks. The authors could only indicate the coexistence of the hypoglycemia and the severe deterioration of the nervous system, since they could not establish which condition was primary.

The diffuse involvement of the brain in our patient, including the cerebellar signs, is in keeping with the neuropathologic reports and is not surprising in view of the fact that he had apparently suffered from hypoglycemia for more than three years. The muscular atrophy which was one of the most striking features of the picture does not seem to have been reported in relationship to spontaneous hypoglycemia. Of course, it is possible that the patient suffered from progressive muscular atrophy coincidentally. The lack of progression following removal of the adenoma may have been a period of quiescence, and the apparent improvement due only to the diminution of the cerebellar component of his disorder. However, the muscular atrophy was noted shortly after the onset of the severe attacks of convulsions, mania and confusion during his hospitalization in the Army. Improvement might well occur if, after relief of the hypoglycemic state, the anterior horn cells which had not been destroyed regained their function. It is to be noted that the physical findings were not fully typical of progressive muscular atrophy. Fibrillations were never noted, and the truncal musculature was involved to the extent of causing a gait similar to that seen in muscular dystrophy. Although no cases have been reported in which destruction of anterior horn cells from hypoglycemia led to the picture of progressive muscular atrophy, Moersch and Kernohan [6] took random sections from the spinal cord of their patients and found that at one segment of the midlumbar involvement about two thirds of the anterior

6. Moersch, F. P., and Kernohan, J. W.: Hypoglycemia: Neurologic-Neuropathologic Studies, Arch. Neurol. & Psychiat. **39**:242 (Feb.) 1938.

7. Blau, A.; Reider, N., and Bender, M. B.: Extrapyramidal Syndrome and Encephalographic Picture of Progressive Internal Hydrocephalus in Chronic Hypoglycemia, Ann. Int. Med. **10**:910 (Dec.) 1936.

horn cells had been replaced by glial proliferation. Winkelman and Moore [8] found changes in the anterior horn cells of cats after repeated induction of hypoglycemic states with insulin. The present case suggests that the changes in the anterior horn cells can continue and produce a picture similar to that seen in progressive muscular atrophy.

Pseudologia fantastica is a condition usually found in charlatans and swindlers and other types of psychopathic personalities who seem capable of deceiving themselves with their falsehoods. The syndrome carried to the extent of fabrication of the entire past history in a manner sufficiently reasonable to deceive a number of physicians is rarely seen. The occurrence as a manifestation of an organic syndrome, and recovery following alleviation of the organic defect is of unusual interest. Bleuler [9] noted in his textbook that he once overlooked the presence of dementia paralytica because of the pseudologia fantastica shown by the patient. The patient's fabrications differed markedly from confabulation such as is seen in Korsakov's syndrome, for they were well organized and carefully defended details, rather than confabulations which arise to fill a memory defect. They did not have the expansive quality of the grandiose delusions of a person with dementia paralytica. Whereas he seemed to act on his fabrications and seemed to have believed them, it is difficult to say that he was really deluded, because of the care he took to avoid being found out and the manipulation of the stories to cover inconsistencies. The pseudologia fantastica appears to have been based on the lowering of his critical ability and the diminution of restraint due to impairment of cortical functioning which permitted repressed personality traits to come to the fore. It may be supposed that the patient's rejection by his family during his early years and his stay in an orphanage had aroused phantasies revolving about the notion that he was really the child of a wealthy mother. There had been some tendencies to act superior to his family and to impress girls by display of affluence prior to his illness, but the traits were counterbalanced by ambition which kept him working steadily. The psychometric studies indicate that, although definite intellectual impairment existed, it was not sufficient to cause disorientation or impairment of memory except during the acute exacerbations of his hypoglycemia. Improvement following his operation was accompanied with disappearance of the confabulated history—a recovery akin to the regression of delusions of patients with dementia paralytica following malaria therapy.

8. Winkelman, N. W., and Moore, M. T.: Neurohistopathologic Changes with Metrazol and Insulin Shock Therapy; and Experimental Study on the Cat, Arch. Neurol. & Psychiat. **43**:1108 (June) 1940.

9. Bleuler, E.: Textbook of Psychiatry, translated by A. A. Brill, New York, The MacMillan Company, 1924.

A symptom which may not have been due to the effect of hypoglycemia on the central nervous system was the episodes of profound weakness on awakening, when he was sometimes unable to move and on other occasions fell to the floor when he tried to arise from bed in the morning. It seems theoretically possible that the excessive sugar metabolism, by depleting the serum potassium, precipitated attacks similar to those seen in periodic family paralysis. Unfortunately, it was not possible to carry out the necessary laboratory studies.

SUMMARY

A case is reported in which long-standing hypoglycemia due to an islet cell adenoma of the pancreas was accompanied with clinical manifestations of widespread damage of the central nervous system, including abnormalities resembling progressive muscular atrophy and cerebellar ataxia, and giving rise to the psychiatric syndrome of pseudologia fantastica. All manifestations, except the residual muscular atrophy, disappeared after removal of the tumor.

METASTATIC MYCOTIC ABSCESSES OF THE BRAIN

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METASTATIC mycotic infections of the brain are not common. At the Mayo Clinic, in a thirty-one year period (1915 through 1945), the lesions of 104 patients with metastatic brain abscesses were studied at necropsy. Brain abscesses due to mycotic organisms were found in only 5 of these cases. Candida (Monilia) albicans was found by culture to be the infecting organism in 1 of these cases. Coccidioides immitis was established histologically in 1 case reported by Beaver and Furrer[1] in 1933. In the case reported by Craig and Dockerty[2] in 1941 these authors were able to culture Coccidiodes immitis from the abscess. In the 2 remaining cases the infections were due to Actinomyces. In view of the fact that the clinical histories and pathologic findings in all these cases were so similar, only 2 of the cases will be reported subsequently in this paper.

Infections and abscesses due to C. albicans are uncommon. A review of the literature shows that the organism has produced some serious lesions in a variety of anatomic locations. Cases of osteomyelitis and infections of the joints have been reported by Keating,[3] Yvin,[4] and Weingart, Wirtz and Irving.[5] Connor[6] in 1933 reported

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Dr. Craig is from the Section on Neurosurgery, Mayo Clinic.

1. Beaver, D. C., and Furrer, E. D.: Pathogenic Yeasts and Yeast-Like Organisms: Report of Case in Minnesota Simulating Coccidioidal Granuloma, J. Lab. & Clin. Med. **18**:329-348 (Jan.) 1933.

2. Craig, W. McK., and Dockerty, M. B.: Coccidioidal Granuloma: A Brief Review with Report of a Case of Meningeal Involvement, Minnesota Med. **24**:150-154 (March) 1941.

3. Keating, P. M.: Fungus Infection of Bone and Joint, South. M. J. **25**: 1072-1078 (Oct.) 1932.

4. Yvin, M.: Un cas de mycose vertébrale, Rev. d'orthop. s. 3, **21**:42-49 (Jan.-Feb.) 1934.

5. Weingart, J. S.; Wirtz, D. C., and Irving, N. W.: Monilia Osteomyelitis: Report of a Case Resulting from Thrush, Am. J. Clin. Path. **12**:597-600 (Dec.) 1942.

6. Connor, J. I.: Chronic Paronychia Due to Monilia, M. J. Australia. **2**:312-314 (Sept. 2) 1933.

13 cases of paronychia due to this organism. Bassler [7] reported a case in which this organism was responsible for splenic and perisplenic abscesses. Mirman [8] had a patient with an infection of the biliary tract due to Candida krusei. Infections of the respiratory tract or the gastrointestinal tract or both have been reported by Reye,[9] Berghausen [10] and Lewis.[11] Reye found, in 150 consecutive autopsies performed on the bodies of children, that 7 deaths were due to esophagitis and 5 of these were caused by C. albicans. Cases of systemic infection with Candida have been reported by many investigators.[12] Cases of endocarditis have been reported by Wikler, Williams, Douglass and Emmons (with Dunn),[13] Joachim and Polayes,[14] Polayes and Emmons,[15] Pasternack,[16] Friedman and Donaldson,[17] and Geiger, Wenner, Axilrod and Durlacher,[18] whose patient also had meningitis

7. Bassler, A.: Fungus Disease of the Spleen: Report of a Case, Rev. Gastroenterol. **12**:413-418 (Nov.-Dec.) 1945.

8. Mirman, J. M.: Moniliasis of the Biliary Tract: Report of Case, J. Lab. & Clin. Med. **19**:379-381 (Jan.) 1934.

9. Reye, D.: Oesophagitis of Infants, M. J. Australia. **2**:673-674 (Dec. 13) 1941.

10. Berghausen, O.: Moniliasis of the Respiratory and Digestive Tract, Am. J. Digest Dis. **3**:271-272, 1936-1937.

11. Lewis, S. J.: Moniliasis of the Lungs and Stomach: Case Report with Autopsy, Am. J. Clin. Path. **3**:367-374 (Sept.) 1933.

12. Nussbaum, S.; Sass, J. A. E., and Rascoff, H.: Systemic Thrush in the Neonatal Period: Report of Case, Arch. Pediat. **58**:689-693 (Nov.) 1941. Wikler, A; Williams, E. G., and Wiesel, C..: Monilemia Associated with Toxic Purpura: Report of a Case, Arch. Neurol. & Psychiat. **50**:661-668 (Dec.) 1943. Warnock, F. B.: Pathogenic Fungi: Studies from Two Fatal Cases, Am. J. M. Technol. **2**:98-105 (May) 1936. Schultz, F. W.: Systemic Thrush in Childhood, J. A. M. A. **105**:650-653 (Aug. 31) 1935. Rockwood, E. M., and Greenwood, A. M.: Monilial Infection of the Skin: Report of a Fatal Case, Arch. Dermat. & Syph. **29**:574-581 (April) 1934.

13. Wikler, A.; Williams, E. G.; Douglass, E. D., and Emmons, C. W.: Mycotic Endocarditis: Report of a Case, J. A. M. A. **119**:333-336 (May 23) 1942.

14. Joachim, H., and Polayes, S. H.: Subacute Endocarditis and Systemic Mycosis (Monilia), J. A. M. A. **115**:205-208 (July 20) 1940.

15. Polayes, S. H., and Emmons, C. W.: Final Report on the Identification of the Organism of the Previously Reported Case of Subacute Endocarditis and Systemic Mycosis (Monilia), J. A. M. A. **117**:1533-1534 (Nov. 1) 1941.

16. Pasternack, J. G.: Subacute Monilia Endocarditis: A New Clinical and Pathologic Entity, Am. J. Clin. Path. **12**:496-505 (Sept.) 1942.

17. Friedman, N. B., and Donaldson, L.: Systemic Mycosis with Mycotic Endocarditis, Arch. Path. **27**:394 (Feb.) 1939.

18. Geiger, A. J.; Wenner, H. A.; Axilrod, H. D., and Durlacher, S. H.: Mycotic Endocarditis and Meningitis: Report of a Case Due to Monilia Albicans, Yale J. Biol. & Med. **18**:259-268 (March) 1946.

and cerebral granulomas due to this organism. Additional cases of meningitis have been reported by Miale,[19] Smith and Sano[20] and Morris, Kalz and Lotspeich.[21] The case of a treated patient who recovered was reported by Zimmerman, Frutchey and Gibbs.[22] Halpert and Wilkins[23] reported a case of suspected meningitis due to C. albicans but did not substantiate their findings by culture of the organism. Their pathologic observations were consistent with those of others describing this entity.

The occurrence of this organism in the healthy human being is not common. In a series of 100 normal young adults Benham and Hopkins[24] failed to culture Candida albicans from the nails or skin, but they did succeed in obtaining 6 positive cultures from the tongue and 18 from the feces.

It is not the purpose in this report to discuss the mycology and pathogenicity of this organism. For this information the excellent studies of Shrewsbury,[25] Benham,[26] Castellani,[27] and Stovall and Pessin[28] should be consulted.

After examination of the reports of cases of C. albicans infection, it was felt desirable to report this case. So far as we know, no other case of brain abscess due to this cause has so far been reported.

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19. Miale, J. B.: Candida Albicans Infection Confused with Tuberculosis, Arch. Path. **35**:427-437 (Mar.) 1943.

20. Smith, L. W., and Sano, M. E.: Moniliasis with Meningeal Involvement, J. Infect. Dis. **53**:187-196, 1933.

21. Morris, A. A.; Kalz, G. G., and Lotspeich, E. S.: Ependymitis and Meningitis Due to Candida (Monilia) Albicans: Report of a Fatal Case of Meningitis, with Comment on Its Clinical, Bacteriologic and Pathologic Aspect, Arch. Neurol. & Psychiat. **54**:361-366 (Nov.-Dec.) 1945.

22. Zimmerman, S. L.; Frutchey, L., and Gibbs, J. H.: Meningitis Due to Candida (Monilia) Albicans with Recovery, J. A. M. A. **135**:145-147 (Sept. 20) 1947.

23. Halpert, B., and Wilkins, H.: Mycotic Meningitis Due to Candida, J. A. M. A. **130**:932-934 (April 6) 1946.

24. Benham, R. W., and Hopkins, A. McH.: Yeastlike Fungi Found on the Skin and in the Intestines of Normal Subjects: A Survey of One Hundred Persons, Arch. Dermat. & Syph. **28**:532-543 (Oct.) 1933.

25. Shrewsbury, J. F. D.: The Genus Monilia, J. Path. & Bact. **38**:313-354 (May) 1934.

26. Benham, R. W.: Certain Monilias Parasitic on Man: Their Identification by Morphology and by Agglutination, J. Infect. Dis. **49**:183-215, 1931.

27. Castellani, A.: A Short General Account for Medical Men of the Genus Monilia, Persoon 1797: Em Bonorden, 1851; Vuillemin, 1911; Castellani and Chalmers, 1919; Pollacci and Nannizzi, 1927, J. Trop. Med. **40**:293-307 (Dec. 1) 1937.

28. Stovall, W. D., and Pessin, S. B.: Pathogenicity of Certain Species of Monilia, Am. J. Pub. Health. **24**:594-602 (June) 1934; Classification and Pathogenicity of Certain Monilias, Am. J. Clin. Path. **3**:347-365 (Sept.) 1933.

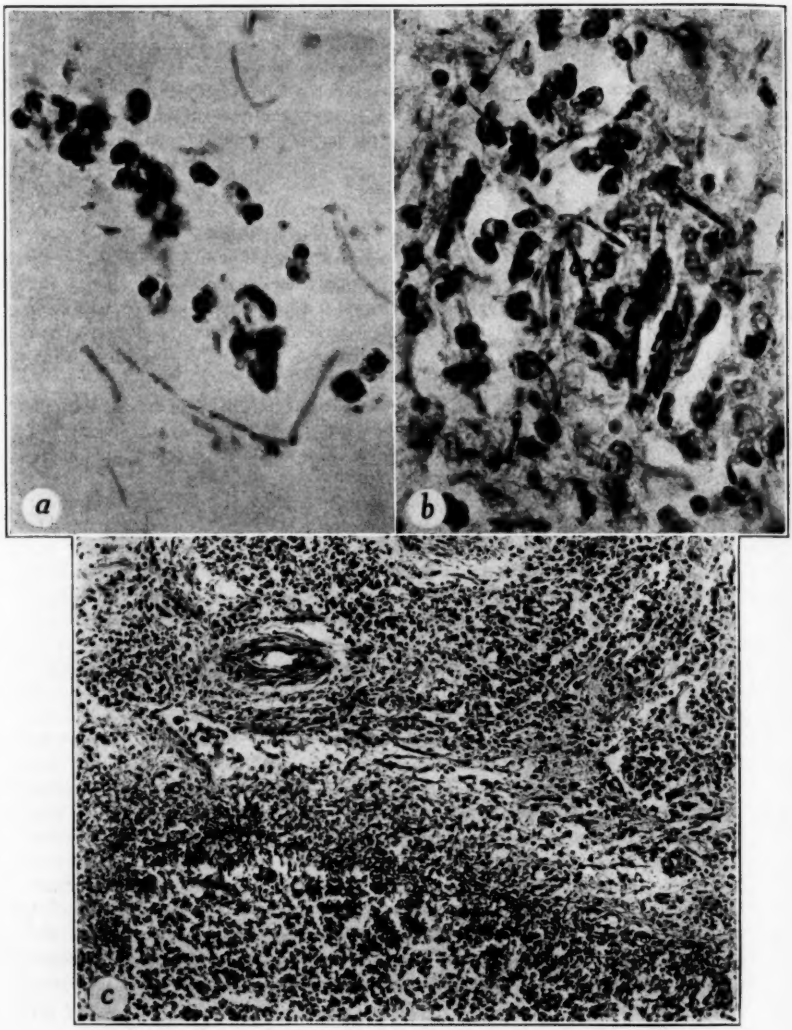
REPORT OF CASES

CASE 1.—A 43 year old man who operated a tavern had been in good health until the early part of February 1941. At that time he experienced malaise, muscular aches and fever. His temperature was reported to have been as high as 101 F. He complained of bilateral frontal headaches. It was thought that he had an acute infection of the upper respiratory tract, since there was an epidemic of such infections at that time. The patient remained in bed for the next two weeks. During the last week in February the headaches increased in severity and were localized primarily to the left frontal region, with extension of the pain to the occipital region. Anorexia and vomiting developed and became increasingly severe. On March 10, 1941, the patient was hospitalized. When a lumbar puncture was performed, the spinal fluid was found to be turbid and under a pressure varying between 270 and 300, expressed in millimeters of water. A pleocytosis was reported; there were 750 cells, consisting of 72 per cent lymphocytes and 28 per cent polymorphonuclear leukocytes, per cubic millimeter of spinal fluid. Tests for globulin gave positive results. No bacteria were found on smears, and no growth occurred on cultures. The value for sugar in the spinal fluid was 62 mg. per hundred cubic centimeters of fluid. The patient was placed on sulfapyridine therapy, and after five days of treatment his condition was essentially unchanged. The presence of a cerebral abscess of the left frontal lobe was suspected, and the patient was referred to the Mayo Clinic for further treatment.

At admission on March 27, 1941, the patient did not appear acutely ill. The positive neurologic findings were bilateral ptosis, slowness of speech and mild loss of memory with a corresponding decrease of intellectual and attentional abilities. There was moderate stiffness of the neck with associated bilateral temporofrontal tenderness on percussion. The right upper extremity revealed approximately 50 per cent loss of motor power and a decrease in muscle tone. There were fibrillary twitches of very small amplitude in the muscles of the right upper extremity. Examination of the reflexes demonstrated a bilateral sucking reflex and increased biceps, brachialis, triceps and supinator jerks in the right upper extremity. The achilles reflex was diminished in the right leg. The abdominal reflexes were absent bilaterally. The Babinski reflex was questionably present on the right. All other reflexes were normal. The examination of the right fundus showed an early papilledema of 1 D. Laboratory studies of the blood and urine gave essentially normal results. An electroencephalogram revealed localization of delta waves in the right frontal area. Spinal fluid obtained by lumbar puncture was cloudy; the pressure was unobtainable because of the poor cooperation of the patient. The results of laboratory analysis of the spinal fluid were as follows: Kolmer test for syphilis, negative; total protein, 100 mg. per hundred cubic centimeters; 150 lymphocytes and 1,600 polymorphonuclear leukocytes with a few erythrocytes per cubic millimeter of fluid; colloidal gold curve 5555321000; sugar, 30 mg., and chlorides, 676 mg., per hundred cubic centimeters. Smears of the spinal fluid were negative for bacteria, yeasts and molds. Inoculation of guinea pigs with spinal fluid gave negative results. The twenty-four and forty-eight hour cultures of spinal fluid were reported negative for bacterial growth. The fourteen day incubated culture was reported positive for C. albicans.

In view of the predominantly right-sided neurologic signs, an abscess of the left frontal lobe was suspected. On March 29, a small cranial opening was made over the left frontal lobe. The dura was tense and when it was opened a large collection of turbid fluid broke through the arachnoid. The brain was not

edematous, and it pulsated normally. A brain cannula inserted into the frontal lobe failed to encounter an abscess cavity. In an encephalogram made immediately after the exploration, the left lateral ventricle, aqueduct and fourth ventricle were not visualized. The subarachnoid spaces were well filled with air and were found to be uniformly dilated. The patient withstood the procedures well, and



Brain abscess caused by C. albicans. (*a*) Organisms in the pyogenic membrane of abscess wall (Brown-Gram stain; × 720). (*b*) Organisms in the inner layer of the abscess wall (hematoxylin and eosin stain; × 800). (*c*) The necrotic core and abscess wall (hematoxylin and eosin stain; × 100).

when he was returned to his room it was noted that he had almost completely recovered from the paralysis of the right upper extremity. He continued to improve daily until the seventh postoperative day, when hiccup developed. Repeated drainage of spinal fluid as well as a trial of promin® (p, p'-diamino-diphenylsulfone-N, N'-didextrose sulfonate) therapy was carried out. The patient continued to fail rapidly in spite of all therapeutic measures and died on the ninth postoperative day.

Necropsy performed with the assistance of Dr. J. W. Kernohan, Section on Pathologic Anatomy, revealed no significant abnormality except in the brain and esophagus. Multiple ulcerations of the esophagus extended into the submucosa and hyphae of C. albicans were seen entwined in the cellular exudate occupying the craters.

The craniotomy site was well healed. There was no evidence of osteomyelitis and no indication that the inferior part of the cerebrum had been injured by extension of disease from the nasal accessory sinuses, which were found to be essentially normal. The dural sinuses were all patent, and the dura was normal in appearance and consistency. The arachnoid was distended by a cloudy spinal fluid and had lost much of its transparency. There was a thick fibrous exudate covering the pons, cerebellum and medulla. The brain was edematous. The convolutions were widened and flattened. The sulci were markedly narrowed. Coronal sectioning of the brain exposed a multiloculated abscess cavity which measured 3.5 cm. in diameter and which communicated with the ventricle in the right frontal lobe. The cavity was filled with a mucopurulent exudate. Grossly, there was poor delimitation of the abscess from the edematous brain tissue which surrounded it. The surrounding white matter was studded with petechial hemorrhages. A careful search was made of the left hemisphere for a pathologic basis for the right monoplegia. No lesion, gross or microscopic, was found. Examination of the left cerebral peduncle failed to reveal grooving of the tentorium which could have accounted for the neurologic findings. The cerebral vessels were all patent. No pathologic process was found in the spinal cord.

Microscopic sections taken through the wall of the abscess demonstrated a well developed reaction to the infection. The abscess cavity was filled with necrotic cellular debris of brain tissue and polymorphonuclear leukocytes. No organisms could be demonstrated in this necrotic core. The inner wall of the abscess consisted of a shaggy membrane composed of young fibroblasts, newly formed capillaries, polymorphonuclear leukocytes and plasma cells. Intermingling with these cells, hyphae of C. albicans were found along with foamy phagocytic cells (figure). Beneath this membrane there was a more highly organized wall consisting of young fibroblasts and fibrous connective tissue. The blood vessels in this lamina showed active proliferation of their endothelial and adventitial coats. The perivascular spaces were filled with lymphocytes and plasma cells associated with macrophages which were stuffed with cellular debris. The surrounding brain tissue showed a moderate degree of astrogliosis, and gemästete astrocytes were common. The white matter was edematous.

Neurologic signs and symptoms which gave a false localization of the abscess in this case can be explained only on the basis of the pressure of encysted cerebrospinal fluid between the arachnoid and pia over the frontoparietal area of the hemisphere opposite the one containing the abscess. This is substantiated by the fact that when this hygroma was revealed and drained, the neurologic signs and symptoms almost entirely disappeared.

Coccidioidal infection of the nervous system generally arises after the development of a generalized systemic form of the disease. Rand [29] in 1930 and Ingham [30] in 1936 each reported a case of spinal meningitis that simulated tumor of the cord. Abbott and Cutler [31] published in 1936 the results of their study of 14 cases of coccidioidal meningitis. They collected reports of 23 such cases from the literature and reported 8 new cases; 6 other cases reported by them previously were included in the reports of 23 cases collected from the literature. Courville and Abbott [32] in 1938 reported a study based on 19 cases of coccidioidal infection of the central nervous system. They found only 2 cases in which lesions involved the central nervous system exclusively. Cases of abscesses of the brain due to coccidioidal infection were reported by Beaver and Furrer [1] in 1933, Craig and Dockerty [2] in 1941 and Rhoden [33] in 1946. It is because of the unusual rarity of this disease that the case of Craig and Dockerty is reported again herein.[34]

Case 2.—The patient was a white 49 year old business man who first registered at the clinic in May 1939, at which time a diagnosis of gout was established. In March 1940, the patient took a two weeks' vacation through southern California. About April 25, 1940, mild occipital headaches of a dull, aching, throbbing nature developed; they were fairly constant but were worse in the morning. They were made worse by bending over or straining, but there was no extension of the headaches. There was no pain or stiffness of the neck. A short time after the development of the headaches he began to notice a dull aching sensation behind the left eye. About May 4, the headaches became more intense and confined the patient to his bed. He remained comfortable as long as he remained at rest, but when he attempted to assume the upright position the headaches became so intense that he was not able to remain up.

On May 9, 1940, the patient was again admitted to the clinic because of persistent headaches and the onset of projectile vomiting. Examination at this time revealed a well developed, well nourished man who did not appear acutely ill. The general examination gave essentially negative results. Neurologic examination revealed some limitation of ocular movements to the left, slurred speech and incoordination of movement in both upper extremities, and the Hoffman reflex was present in the right upper extremity. Funduscopic examination gave

29. Rand, C. W.: Quoted by Ingham.[30]

30. Ingham, S. D.: Coccidioidal Granuloma of the Spine with Compression of the Spinal Cord, Bull. Los Angeles Neurol. Soc. **1**:41-45 (March) 1936.

31. Abbott, K. H., and Cutler, O. I.: Chronic Coccidioidal Meningitis: Review of the Literature and Report of Seven Cases, Arch. Path. **21**:320-330 (March) 1936.

32. Courville, C. B., and Abbott, K. H.: Pathology of Coccidioidal Granuloma of the Central Nervous System and Its Envelopes, Bull. Los Angeles Neurol. Soc. **3**:27-41 (March) 1938.

33. Rhoden, A. E.: Coccidioidal Brain Abscess, Bull. Los Angeles Neurol. Soc. **11**:80-85 (March-June) 1946.

34. This case report is republished, with permission, from Craig, W. McK., and Dockerty, M. B.: Coccidioidal Granuloma: A Brief Review with Report of a Case of Meningeal Involvement, Minnesota Med. **24**:150-154 (March) 1941.

negative results. Laboratory studies of the blood and urine gave values that were within normal limits. Roentgen studies of the head and thorax revealed no significant abnormalities. A lumbar puncture done on May 10 demonstrated an initial pressure of 160, expressed in millimeters of water. The spinal fluid was clear. The spinal fluid studies showed a total protein content of 40 mg. per hundred cubic centimeters of fluid and a cell count of 6 lymphocytes per cubic millimeter. On May 11, the patient's headaches had become greatly increased, and his speech disturbance and incoordination were much more pronounced. A diagnosis of acute increased intracranial pressure was made, and ventricular aspiration and drainage were performed to relieve the critical situation.

The immediate postoperative course was definitely improved. The patient was free of headaches and his speech became normal; however, the incoordination of the upper extremities was not relieved. Because of the clinical course and findings in this patient, the presence of a space-occupying lesion in the posterior fossa was suspected, and on May 14, a bilateral cerebellar craniotomy with decompression was performed by one of us (W. McK. C.). At the time of the operation it was noted that both cerebellar tonsils were herniated through the foramen magnum and the convolutions of the left cerebellar hemisphere were flattened. Exploration of this flattened cerebellar hemisphere revealed a large abscess which was evacuated and drained. The surgical pathologic diagnosis was a coccidioidal cerebellar abscess. The dura was closed, with drainage, and the patient returned to his room in excellent condition. Tissue removed at the time of operation was cultured on blood agar and C. immitis was isolated, which confirmed the surgical pathologic diagnosis made by Dr. Dockerty. The patient was placed on chemotherapy, but his course was disappointing. He became more acutely ill and died, in spite of supportive measures, on the thirty-first postoperative day.

The findings at necropsy included an abscess of the left cerebellar lobe that measured 1 by 1 by 0.5 cm. which was well encapsulated. Sections of this abscess were taken for microscopic study. There was a well developed collagenized wall, with plasma cells and neutrophils, among which the Coccidioides could be noted. Budding forms were not noted but spores were found. The only other pathologic finding of interest was that of well developed multiple coccidioidal granulomas of both lungs.

SUMMARY

Two of 5 cases of mycotic abscesses of the brain have been reported in detail. These 2 cases represent 4.8 per cent of 104 metastatic brain abscesses studied at the clinic. It is difficult to accept this figure as being representative of the incidence of mycotic abscesses of the brain. Approximately one third of the cultures taken from 104 metastatic brain abscesses studied by Gates, Kernohan and Craig [35] were reported as negative for micro-organisms. This could be explained by the fact that many patients were intensively treated by chemotherapeutic and biologic agents before cultures were taken; however, it is felt that greater care should be exercised in the culturing of cerebral abscesses for molds and yeasts, and that the material selected for culturing should be part of the abscess wall rather than the necrotic debris from the abscess cavity.

35. Gates, E. M.; Kernohan, J. W., and Craig, W. McK.: Metastatic Brain Abscess, unpublished data.

MEDULLOBLASTOMA OF THE CEREBELLUM

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THE RESULTS of treatment of medulloblastoma of the cerebellum as reported in the literature have been uniformly depressing.[1] When Bailey and Cushing first segregated this neoplasm from the general group of gliomas, the average life expectancy for patients treated by operation alone was about seven months; the addition of postoperative irradiation extended the average survival from onset of symptoms to seventeen to nineteen months. With improved radiation technics, the average survival was increased to two or three years. However, cases

From the Department of Roentgenology, University Hospital, University of Michigan.

1. (*a*) Bailey, P., and Cushing, H.: Medulloblastoma Cerebelli, Arch. Neurol. & Psychiat. **14**:192-224 (Aug.) 1925; (*b*) The Tumors of the Glioma Group, Philadelphia, J. B. Lippincott Company, 1926, pp. 121-122. (*c*) Olivecrona, H., and Lysholm, E.: Notes on the Roentgen Therapy of Gliomas of the Brain, Acta radiol. **7**:259-268, 1926. (*d*) Bailey, P.; Sosman, M. C., and Van Dessel, A.: Roentgen Therapy of Gliomas of the Brain, Am. J. Roentgenol. **19**:203-264 (March) 1928. (*e*) Grant, F. C.: A Clinical Study of Midline Cerebellar Tumors in Children, S. Clin. North America **9**:1155-1168 (Oct.) 1929. (*f*) Bailey, P.: Further Notes on the Cerebellar Medulloblastomas: The Effect of Roentgen Radiation, Am. J. Path. **6**:125-136 (March) 1930. (*g*) Cushing, H.: Experiences with the Cerebellar Medulloblastomas, Acta path. et microbiol. Scandinav. **7**:1-87, 1930. (*h*) Tracy, F. E., and Mandeville, F. B.: Roentgen Therapy of Medulloblastoma Cerebelli, Radiology **17**:259-265 (Aug.) 1931. (*i*) Alpers, B. J., and Pancoast, H. K.: The Effect of Irradiation of Normal and Neoplastic Brain Tissue, Am. J. Cancer **17**:7-24 (Jan.) 1933. (*j*) Elsberg, C. A., and Gotten, N.: The Results of Conservative Compared with Radical Operation in the Cerebellar Medulloblastomas, Bull. Neurol. Inst. New York **3**:33-53 (June) 1933. (*k*) Brody, B. S., and German, W. J.: Medulloblastoma of the Cerebellum: A Report of Fifteen Cases, Yale J. Biol. & Med. **6**:19-30 (Oct.) 1933. (*l*) Cutler, E. C.; Sosman, M. C., and Vaughan, W. W.: The Place of Radiation in the Treatment of Cerebellar Medulloblastomas, Am. J. Roentgenol. **35**:429-453 (April) 1936. (*m*) Sachs, E.; Rubinstein, J. E., and Arneson, A. N.: Results of Roentgen Treatment of a Series of One Hundred Nineteen Gliomas, Arch. Neurol. & Psychiat. **35**:597-616 (March) 1936. (*n*) Tarlov, I. M.: Effects of Roentgenotherapy on Gliomas, ibid. **38**:513-536 (Sept.) 1937. (*o*) Alpers, B. J.; Pender-

(Footnote continued on next page)

of longer survival have been reported.[2] The exact number of such cases is difficult to determine from the data presented in the literature. Many of the pertinent cases appear in more than one report without exact identification; often the survival status is not clearly given. There appear to be approximately 27 patients who survived more than three years. Of these, apparently 12 were alive three to nine years after treatment, presumably without clinical evidence of disease. It is impossible to determine the total number of patients from which these 27 came. In general, the literature has dealt with prolongation, rather than with the saving, of life in patients with this tumor. For adult patients, according to the report of Spitz, Shenkin and Grant,[2r] the outlook seems more favorable: Three of 21 patients were alive three, six and eight years, respectively, after treatment, with 10 other patients surviving three to seven years after treatment. However, in the age group of 16 years or less, none of 60 patients survived more than three and one-half years. At the University Hospital, because of consistently poor results in the treatment of this disease, the method of postoperative irradiation was revised in 1938 and this modification has continued to be in use up to the present time. During this period, 25 patients with medulloblastoma of the cerebellum were treated, and their cases form the basis of this report.

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grass, E. P., and Chamberlain, G. W.: The Effects of Irradiation on Gliomas, Am. J. Roentgenol. **38**:203-238 (July) 1938. (*p*) D'Errico, A.: Diagnosis and Treatment of the Medulloblastoma of the Brain, Texas State J. Med. **35**:475-478 (Nov.) 1939. (*q*) Baker, A. B.: Intracranial Tumors, Minnesota Med. **23**:669-703 (Oct.) 1940. (*r*) Mandeville, F. B.; Russell, D. A., and Farley, M. S.: Roentgen Therapy of One Hundred Consecutive Tumors of the Brain, Radiology **37**:560-568 (Nov.) 1941. (*s*) Smith, W. A., and Fincher, E. F.: Intracranial Tumors in Children, South. M. J. **35**:547-555 (June) 1942. (*t*) Pendergrass, E. P.; Hodes, P. J., and Godfrey, E. W.: The Radiation Treatment of Cerebellar Medulloblastomas, Am. J. Roentgenol. **48**:476-490 (Oct.) 1942. (*u*) Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1944, pp. 785-788.

2. (*a*) Bailey and Cushing.[1a,b] (*b*) Bailey, Sosman and Van Dessel.[1d] (*c*) Bailey.[1f] (*d*) Cushing.[1g] (*e*) Elsberg and Gotten.[1j] (*f*) Brody and German.[1k] (*g*) Cutler, Sosman and Vaughan.[1l] (*h*) Sachs, Rubinstein and Arneson.[1m] (*i*) Alpers, Pendergrass and Chamberlain.[1o] (*j*) D'Errico.[1p] (*k*) Mandeville, Russell and Farley.[1r] (*l*) Smith and Fincher.[1s] (*m*) Pendergrass, Hodes and Godfrey.[1t] (*n*) Ford.[1u] (*o*) Ingraham, F. D., and Bailey, O. T.: Cerebellar Medulloblastoma with Verification Nineteen Years After the Onset of Symptoms, J. Neurosurg. **1**:252-257 (July) 1944. (*p*) Ingraham, F. D.; Bailey, O. T., and Barker, W. F.: Medulloblastoma Cerebelli; Diagnosis, Treatment and Survivals with a Report of Fifty-Six Cases, New England J. Med. **238**:171-175 (Feb. 5) 1948. (*q*) Penfield, W., and Feindel, W.: Medulloblastoma of the Cerebellum, with Survival for Seventeen Years, Arch. Neurol. & Psychiat. **57**:481-485 (April) 1947. (*r*) Spitz, E. B.; Shenkin, H. A., and Grant, F. C.: Cerebellar Medulloblastoma in Adults, ibid. **57**:417-422 (April) 1947.

PRESENT STUDY

Each patient was subjected to operation and, subsequently, to irradiation. Examination of tissue removed at operation established an unequivocal diagnosis of medulloblastoma for each of the 25 patients. The surgical procedures varied from biopsy (1 patient) to gross total removal; in most of the patients, the removal was as extensive as was considered feasible from a surgical standpoint.

The scheme of postoperative irradiation was designed (1) to irradiate the entire cerebrospinal axis in a segmental fashion, beginning with the primary site, (2) to deliver a moderately large dose of roentgen radiation to each segment and (3) to complete the treatment of each segment in a relatively short time. Treatment was begun as soon as the incision was well healed unless some postoperative complication made further delay advisable. The average interval between operation and irradiation was about ten days.

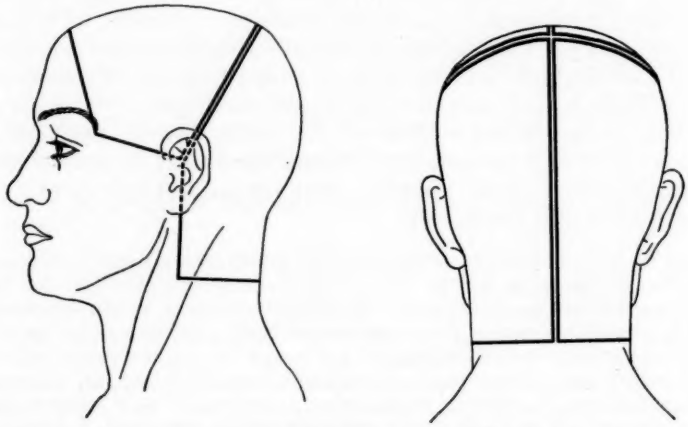

Fig. 1.—Diagrammatic representation of the four fields used for irradiation of the cranial cavity in cases of medulloblastoma of the cerebellum.

Two fields were used in irradiation of the posterior half of the skull (fig. 1); the inferior borders extended below the occipital bone onto the posterior surface of the neck. The anterior half of the skull was irradiated by a second pair of lateral fields. The distance, from the lower margins of the fields of the posterior half of the skull to the coccyx, was divided into three fields (7 to 12 cm. wide), so that the entire subarachnoid system of the spinal axis was irradiated.

On the first day, 250 r (measured in air) was delivered to one of the fields of the posterior half of the skull; on the second day and thereafter, 250 r was administered to each of two fields. The fields in the posterior half of the skull were treated daily until a dose of 1,750 r per field was attained. The next segment, the anterior half of the skull, was then treated in the same fashion to the same total dose. The third segment, which consisted of the upper two spinal fields, was treated next, at the same daily rate, to the same total dose. The lowest spinal field was treated by itself during the last seven days. In some patients, if the high daily dose had been fairly well tolerated, the dose to the fields of the posterior half of the skull was increased by irradiating one of these

fields along with irradiation of the last spinal field, alternating treatment to the right and the left side on successive days and raising the total dose to 2,000 r or more to each field. The entire course of treatment required four and one-

Data on 25 Patients with Medulloblastoma of Cerebellum Treated by Irradiation

Case No.	Sex	Age, Yr.	Duration of Signs or Symptoms, Mo.	Extent of Lesion	Survival Period, Mo.
			Patients Who Died		
1	F	4	1.0	Extensive	1
2	M	3	0.5	Moderately extensive	3
3	M	11	3.0	Extensive	3
4	F	3	3.0	Extensive	5
5	F	6	3.0	Extensive	7
6	M	2	0.5	Moderate	7
7	M	11	4.0	Extensive	8
8	M	34	1.5	Extensive	10
9	M	9	1.0	Extensive	12
10	M	8	2.0	Extensive	14
11	M	31	5.0	Extensive	17
12	M	7	3.0	Extensive	19
13	M	9	8.0	Moderately extensive	24
14	M	12	4.5	Extensive	26
15	M	37	2.0	Moderate	28
16	M	8	3.0	Moderate	34
17	M	10	1.5	Extensive	38
18	F	7	2.0	Extensive	68
			Patients Alive		
19	F	8	4.0	Extensive	33 (Excellent health; no apparent neurologic difficulty)
20	F	3	2.0	"Plastic arachnoiditis"	47 (Excellent health; no apparent neurologic difficulty)
21	M	4	1.0	Extensive	50 (Excellent health; no apparent neurologic difficulty)
22	M	12	4.0	Extensive	70 (Excellent health; mild ataxia; good student)
23	M	14	1.5	Extensive	72 (Good health)
24	F	18	3.0	Moderately extensive	83 (Good health; mild ataxia; school teacher)
25	F	9	4.0	Extensive	92 (Intermittent headaches first 4 years; intermittent convulsions last 3¼ Years

half to five weeks. No additional irradiation was given, unless evidence of recurrence developed. The voltage was 200 kilovolts (Villard circuit), and half-value layer of 0.9 mm. of copper, with added filtration of 0.5 mm. of copper and 1.0 mm. of aluminum, was used at a distance of 50 cm.; the output was about 50 r a minute as measured in air.

Of the 25 patients treated, 18 are dead and 7 (28 per cent) are alive, at the time of this report. The shortest survival time in the group of patients who are living is thirty-three months and the longest ninety-two months; the other 5 patients are alive forty-seven, fifty, seventy, seventy-two and eighty-three months, respectively, after treatment (table; fig. 2). Of the patients who did not survive, 9 died within the first year after treatment; 13 died within two years and 16 within three years. One patient died thirty-eight months, and 1 sixty-eight months, after treatment (table; fig. 2).

With 1 exception, the 7 surviving patients are in good condition (table). Two patients, who are otherwise in good health, have mild ataxia; 1 is a student and is doing good work; the other is a school teacher. Four patients are apparently free of any significant neurologic difficulty. The patient (case 25) who is living after ninety-two months suffered from intermittent headaches for the first four years after treatment; and for the last three and one-quarter years she has had intermittent convulsions. Despite this, we do not believe that the neoplasm has recurred. Experience with the 18 patients who died of

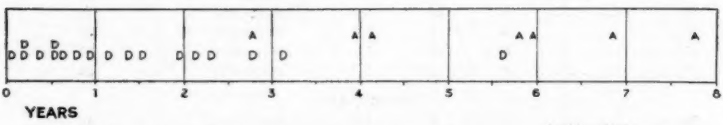

Fig. 2.—Graph showing duration of survival of 25 patients with medulloblastoma of the cerebellum. *D* denotes time of death after treatment; *A*, period of survival of patients who are alive.

recurrences has shown that death takes place shortly after symptoms of recurrence develop. This is true with or without additional treatment. Probably the convulsions are due to damaged nerve tissue consequent to the surgical procedure or to damage to blood vessels from irradiation. None of the 7 surviving patients received any surgical or radiation treatment other than the initial operation and the course of irradiation given shortly afterward.

The neoplastic involvement in the 7 patients who are alive was as extensive as in the patients who did not survive (table). In 1 patient (case 20) the findings at operation were atypical and were interpreted as diffuse "plastic arachnoiditis." Because of this, the operation was limited to the removal of a bit of tissue for microscopic examination. It is significant, from the point of view of the potentialities of radiation therapy of this disease, that this patient is alive and well, forty-seven months after treatment.

The ratio of males to females among the 25 patients is 17:8. For the patients who died it is 14:4; for the survivors it is 3:4. Although

the sex ratio appears to differ, the numbers are too small to exclude the possibility of sampling variation as the explanation of this phenomenon. The average age (11.8 years) of the patients who died is somewhat higher than that of the survivors (9.7 years), but the difference is not statistically significant. The average duration of symptoms for each of the two groups is nearly the same—2.4 and 2.7 months.

No patient in whom recurrence or metastasis developed has remained alive, even though additional radiation treatment was given. In nearly every patient recurrence presaged death in a short time. Eight of the 18 patients who died were free from symptoms for a year or more before recurrence developed. Three were in good condition for two to two and one-half years, and 1, for four years. The inability to exercise any significant control over the disease when recurrence develops emphasizes the fact that the initial therapeutic effort must succeed in wiping out the neoplasm; otherwise, failure is certain.

In figure 2 is plotted the duration of survival for each of the patients who died (*D*) and for those who are living (*A*). Seventeen of the 18 nonsurvivors died within the first thirty-eight months after treatment. This suggests that any patient who is alive without evidence of disease a little more than three years after treatment has an excellent chance of survival. The death sixty-eight months after treatment, however, indicates that a threat still exists.

Contrary to the forbiddingly gloomy picture seen in the reports contained in the literature, which has caused medulloblastoma of the cerebellum to be considered as an inevitably fatal disease, the experience embodied in these 25 cases suggests that such is not necessarily the case. The worst construction that can be placed on the survival data in this group is to assume that the 3 patients who are living less than five years after treatment will die before the five year mark has been reached (the data shown in figure 2 make this assumption unlikely) and that the patient living ninety-two months after treatment (case 25) represents a worthless result and is, perhaps, to be grouped with those who die before five years. This leaves 3 of 25 patients alive and well at five years—a "cure" rate of 12 per cent. Low as this figure is, it represents an element of hope, in contrast to most of the data reported to date. Moreover, this low figure exceeds what can be accomplished in treatment of a number of other malignant neoplasms by any method. The internal character of the survival data, however, indicates that the construction just mentioned is too severe. The actual survival rate at five years is 16 per cent, if the patient (case 18) who died at sixty-eight months is counted as dead at five years; and there seems to be a good chance that it may become as high

as 28 per cent, if patients 19, 20 and 21 (table) continue in their present condition.

In the case of numerous other malignant neoplasms, survival without evidence of disease at five years after treatment is considered satisfactory evidence of clinical cure. Of course, while accepting this as a good working basis, one realizes that "cure" at five years is not necessarily conclusive evidence of absolute eradication of a neoplasm. Nevertheless, there seems to be no valid reason for not applying this generally accepted criterion to the cerebellar medulloblastoma. Indeed, the chronologic distribution of survival among the patients who died and those who are still living, shown in figure 2, with the relatively sharp segregation in time of the two groups, points to its especial validity in this disease. It is entirely possible that this neoplasm may be curable and survival percentages may be obtained that compare favorably with those for other malignant growths and exceed those obtained for many.

The question must be raised regarding the role of surgery and of irradiation in obtaining such results. There are two lines of evidence that point conclusively to the ineffectiveness of surgery and to the effectiveness of irradiation. No substantiated report could be found of a patient who was living and well more than three years after treatment when surgical removal was the sole therapy. In most cases in which treatment was surgical only, recurrence and death occurred within one year. Longer survivals were not obtained until postoperative irradiation was included. On the other hand, the survival periods obtained for the 25 patients reported here point, without equivocation, to the potency of irradiation. To fortify this contention, one may point to case 20. No surgical excision was performed in this case; only a biopsy was done. With only irradiation, the patient is living and free of evidence of disease, forty-seven months after treatment.

If one accepts the present report as evidence of the possibility of cure of medulloblastoma of the cerebellum by radiation therapy, there is a clear indication for deemphasizing the role of surgery in this disease. Improvement in results can be accomplished only by better radiation technics. The essential problem, therefore, is the development of more efficient irradiation methods; concentration of effort in this direction is necessary. The basic difficulty in the treatment of this disease rests on the necessity of irradiating a large part of the body in order to destroy all the neoplastic foci.

SUMMARY

The results in 25 patients with medulloblastoma of the cerebellum treated by surgical removal followed with vigorous postoperative irradiation are reported. Eighteen patients were dead (17 at thirty-eight

months or less, and 1 at sixty-eight months, after treatment). Seven (28 per cent) were alive, without evidence of neoplasm, thirty-three, forty-seven, fifty, seventy, seventy-two, eighty-three and ninety-two months after treatment. Six of the 7 patients were in good clinical condition.

In 1 patient, the only surgical procedure performed was biopsy; this patient was living and well forty-seven months after treatment.

The evidence suggests that medulloblastoma of the cerebellum may be a curable disease and that cure is possible only with irradiation.

University Hospital.

THE SYNDROME OF SENSORIMOTOR INDUCTION IN DISTURBED EQUILIBRIUM

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THE FINDING of changes in sensory function in patients with disturbed equilibrium is of much theoretic and practical significance, opening up new aspects of neurologic research. Observations hitherto reported are, however, too few to disclose the whole clinical complex and the underlying pathologic mechanism. The broadening of the clinical concept and the establishment of a solid basis of confirmed facts are particularly required, and the following observations may serve as a contribution.

CLINICAL OBSERVATIONS

CASE 1.—*General Clinical Picture.*—J. W., an engineer aged 29, had developed normally as a child. He had always been healthy.

The present disease began nine months before his admission. He noticed that when he walked he bumped into people and objects on his right and that involuntarily he deviated to the right. A few months later he also noted great fatigue when reading, and the print seemed to swim before his eyes. He then found that he was constantly making mistakes in drawing and measuring. He complained of constant nausea from the onset of his illness, but his general condition was good.

Neurologic examination on admission showed a delayed reaction of the pupils to light: free, spontaneous movement of the eyes, and fine nystagmoid movements on extreme fixation to the right. There were moderate weakness of innervation of the angle of the mouth on the right, diminution in strength of the abdominal reflexes on the left side and a series of disturbances of body posture and sensory functions, to be discussed in detail later. In all limbs, power, active and passive movements and all modalities of superficial and deep sensibility, including stereognosis, were normal. Examination of the reflexes revealed no abnormality except for decrease in strength of the abdominal reflexes on the left.

Ophthalmologic examination (Professor Feigenbaum) showed that both papillae were clearly demarcated but pale, due to simple optic nerve atrophy. There was concentric contractions of the visual fields for white and colors. The right visual field was contracted on all sides by 25 degrees except in the outer upper quadrant, the limit there being 30 degrees, and the left visual field was contracted by 20 degrees. Astigmatism was not noted. Otologic examination (Dr. Lachmann) showed normal hearing on each side and a normal vestibular reaction to caloric and rotary tests. Roentgenographic study of the skull and examinations of the blood and spinal fluid revealed no abnormality.

Special Studies.—Disturbances of Body Posture and Equilibrium: The patient inclined his head to the right without being aware of it. Any alteration from this

position was felt as unpleasant. When the patient's head was passively bent to the left and he was asked to return it to the midline with his eyes shut, he always went beyond the midline and returned to his usual posture. When the patient's head was passively inclined to the extreme right, he reverted to his primary position without reaching the midline at all. When the patient was asked to keep his eyes shut, the inclination of the head to the right appreciably increased and was followed by inclination of the whole body. When asked to keep his arms stretched out forward at the same level he was able to do so, but the strain was obvious. However, when he was asked to stretch out his arms with the eyes shut, the right arm slowly rose about 30 cm., at the same time deviating slightly outward, while the left arm descended with a rocking movement 15 to 20 cm. (fig. 1 *A*). The same results were noted when the arms were examined separately. Lifting of the right arm and lowering of the left were also seen when he was asked to stand with his eyes shut and to stretch out his arms sideways at the same

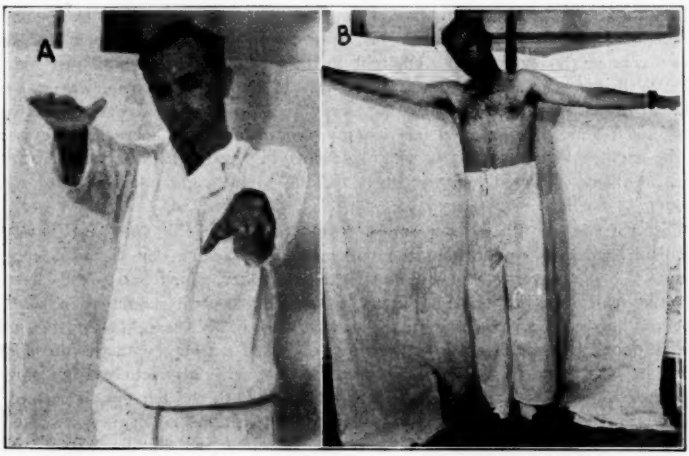

Fig. 1 (case 1).—Patient with eyes closed and arms lifted.

level (fig. 1 *B*). The patient was always completely unaware of the lifting of the right arm. When the left arm only was stretched out and it descended the patient was again completely unaware of its falling. When both arms were tested, he was aware of lowering the left arm only by a feeling of "lightness," as he put it, in his right arm. When the patient with his eyes shut had one arm lifted by the examiner to any given level and was then asked to lift the other arm to the same level, the result was that his right arm was always placed too high and the left arm too low.

With eyes open, the patient pointed equally well with either arm in any direction. When the patient with his eyes shut was asked to perform the finger-nose test in a vertical plane, his right arm deviated to the right, while he performed the test with his left arm in a normal manner. When the test was done in a horizontal plane, that is, with the arms stretched sideward, then the right arm was placed too high and the left arm too low. This effect became more obvious as the test was repeated. When the patient with his eyes shut was

asked to point out the midline of his body, he did it accurately with his left arm, but with his right arm he was short of the midline by 4 to 5 cm. When he lay with his eyes shut and was asked to raise both his legs, the right leg deviated to the right and was lowered; the left leg, however, fell more quickly than the right. When asked to lift one leg to the same level as the other, he always placed his right leg higher and his left leg lower.

When he stood with his eyes open, a slight inclination of his body to the right was noticeable. With his eyes shut the inclination increased, but the patient was unaware of this until he was about to fall. Changing the position of the head, e. g., inclining it to the left, had no effect on the tendency to fall. The patient stated that since the onset of his illness he had had to take special care when walking, because he would otherwise fall to the right. To keep his balance when walking, he had to shift his weight to the left. Occasionally, when he failed to pay attention to his walking, he had to put his left leg across his right in order to avoid falling. In the dark, walking was specially difficult, because his efforts to keep his balance did not counteract the tendency to fall to the right and achieve a steady gait. With his eyes open, the patient seemed to walk rather confidently, even though a slight inclination to the right was just noticeable. With his eyes shut he deviated strongly to the right when he was walking forward or backward. When he was asked to go to and fro five times between two fixed points, he zigzagged increasingly, but always with increasing deviation to the right. When asked to walk sideward in a straight line with his eyes shut, he always deviated forward when walking to the right and backward when walking to the left.

Disturbances of Visual Perception: About four months after the onset of his disturbances of equilibrium, the patient became aware that he made visual errors. When inspecting a newly constructed wall, he pointed out to the laborers that the wall was not quite straight. Only after control examination with a gage did he become convinced that the wall was really straight. At the same time he found himself making further mistakes when working with the theodolite. When he was gaging a geometrically straight line with his right eye, he saw it as shifted to the right, and when he was gaging it with the left eye, it seemed to shift to the left. After having compared results with his colleagues, he had to admit that this deviation was an optical illusion. He found that the extent of his subjective parallax was 6 degrees and corrected for it thereafter. The patient stated that he then saw each closed room as though it were in perspective. The opposite wall seemed to be smaller, while the side walls, the ceiling and the floor seemed to incline to each other in the direction of the opposite wall, and they appeared to overlap at not too great a distance.

When the patient was asked to draw a vertical line, he drew it with its upper end inclining to the right (fig. 2*a*). When a truly vertical line was shown to him, he saw it with its upper end deviating to the left (fig. 2*b*). When a line deviating 6 degrees to the right was shown to him, he saw it as vertical.

When he was asked to draw a horizontal line, he drew it with its right end tilted upward (fig. 2 *c*). When he was shown a truly horizontal line, he saw it with its right end inclining downward (fig. 2 *d*). A line drawn tilting upward 6 degrees at its right end was seen by him as horizontal.

These subjective visual errors concerned only one end of the line, while the other end served as a fixed point. When he was asked, however, to gage the middle of the line, it appeared to him as though it were rotated about its central point. The horizontal line seemed to be turned clockwise and the vertical line counterclockwise (fig. 2 *e* and *f*).

The outline of the vertical and horizontal lines did not appear to him to be double or bent, but the line as a whole was displaced. These deviations were always observed quite independently of whether he was looking with the right eye or with the left eye only or with both eyes. Likewise, the degree of deviation was always the same. A change in the position of the head also did not influence the constancy and degree of these deviations.

When asked to draw a right angle, the patient always drew an acute angle. In accordance with the basic deviations shown in the preceding paragraph, a right angle in the first quadrant appeared to him to be an obtuse angle of 102 degrees

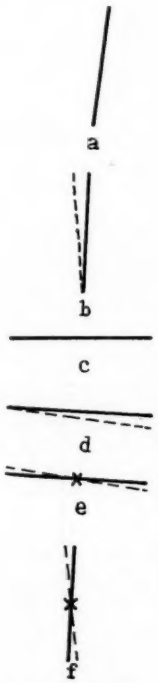

Fig. 2 (case 1).—Displacement of vertical and horizontal lines as seen with either or with both eyes.

(fig. 3 *a*), and an acute angle of 78 degrees, to be a right angle. A right angle cross deviated in such a way that the upper angle in the first quadrant and the opposite one, in the third quadrant, appeared to him to be obtuse angles, while the upper angle in the second quadrant and the opposite one, in the fourth quadrant, appeared to be acute angles (fig. 3 *b*). A square appeared to him to be a rhombus, the vertical sides being inclined to the left and the horizontal lines inclined downward to the right (fig. 3 *c*). A rectangle appeared to him to be a parallelogram (fig. 3 *d*). On the contrary, a rhombus or a rectangle the vertical lines of which were inclined to the right and the horizontal lines inclined upward to the right

appeared to him as a square or a rectangle. Spherical structures were seen normally.

Two vertical parallel lines he saw as though they came together at their upper end. Two lines drawn as diverging at their upper ends were perceived by him as parallel. Two horizontal parallel lines appeared to him to approximate on the left. When he was asked, however, to gage the lines from the left side, he saw them approximating on the right. When the vertical and horizontal parallel lines were closed at one end by a third line, he saw them again as a parallelogram.

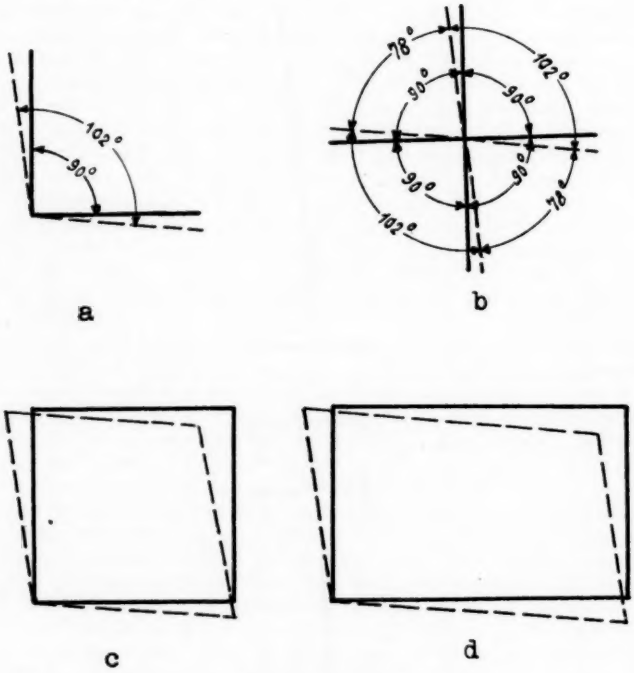

Fig. 3 (case 1).—Subjective deviation of geometric figures. Solid lines show the actual picture; broken lines, the subjective perception.

The same impression of horizontal lines approximating he experienced when reading. When reading Hebrew, which is printed from right to left, he saw the lines approaching one another at the left; when he was reading Latin, with script from left to right, the lines seemed to approach one another on the right.

All these deviations were also seen constantly when colored lines were shown him. Yet the patient had a sure eye when estimating dimension or distance. The well known optical illusions and tricks were easily recognized as such at once.

The handwriting of the patient had become larger since the onset of his illness. When he wrote with his eyes open, there was a marked tendency for

the writing to incline upward. This tendency was more evident when he was writing with his eyes shut (fig. 4 *a* and *b*) and was present for Hebrew (*a*) and Latin (*b*) script.

About the time that the patient became aware of his visual errors, he found that he confused his colored pencils when working. At length he had specially to mark his colored pencils when drawing. A detailed examination revealed that of all colors he could recognize accurately only three: black, white and red. The following extract from his case sheet is illustrative:

Object	Color Matched by the Patient
Green leaves	Blue
Blackboard	Black
Grass	Blue
Ink	Black
Gold	Gray
Snow	White
Orange	Gray
Paper	White
Sky	Green
Blood	Red

When samples of colors were shown him, he likewise recognized only black, white and red. All other colors were not recognized as such, but were described only as being darker or lighter than these. For example, he described blue as

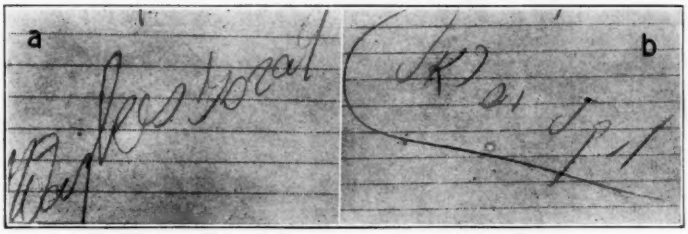

Fig. 4 (case 1).—Upward slanting of Latin script (*a*) and of Hebrew script (*b*).

"light black," pink as "light red," yellow as "dark white," violet as "dark dark white" and green as "light light black." The same findings were obtained with the colors of the spectrum. The red part of the spectrum from 685 to 595 angstrom units he described correctly as red, while the yellow and green part, from 595 to 535 angstrom units, was perceived as gradations of white and the blue part, from 535 to 485 angstrom units, throughout as black.

These findings were obtained when he was looking with both eyes or with one eye alone and on his changing the position of the head. The test with Stilling's colored tables proved this dissolution of color perception to be of organic origin.

Disturbances of Perception in Tactile and Haptic Spheres: When a small rod was placed vertically in the middle of the patient's chest, it seemed to him that it inclined upward to the left. When the rod was placed with the inclination to the right, it seemed vertical. When the rod was placed first on the left and then on the right side of his chest, the inclination to the left seemed more pronounced in the latter position. When two parallel rods were placed on his chest, they seemed to approximate at their upper ends. When the rod was placed horizontally on his chest, it seemed to be inclined upward to the right. Only when the rod was placed inclined downward to the right did it seem to be horizontal. When a ring was pressed on the middle of his chest, the left half seemed to be quite circular, but the right half seemed ovoid.

When the patient with his eyes closed was asked to place a rod vertically, he always placed it with its upper end inclined forward to the right (fig. 5 *A*). When this test was repeated with each hand separately, the deviation was greater with his right hand. When asked to place a rod horizontally, he placed it with its right end downward (fig. 5 *B*). A rod placed vertically in his hands seemed to be inclined upward to the left and a rod placed horizontally seemed inclined upward to the right.

Course of the Disease.—In the course of time the patient's condition improved appreciably. About seven months after the aforedescribed abnormalities were found and confirmed on repeated examination, the patient became aware of a progressive change for the better in his equilibrium. He then walked much more confidently and steadily, without having to pay special attention. At the same

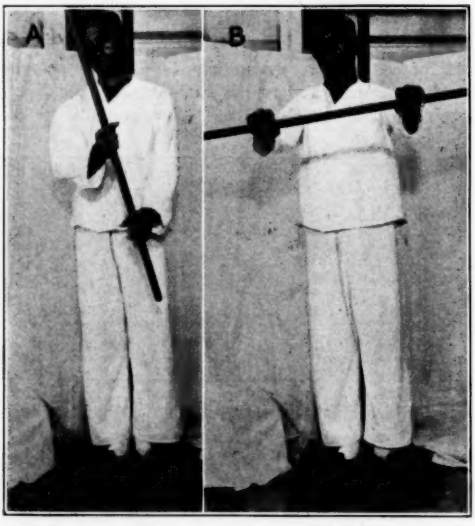

Fig. 5 (case 1).—Deviation of a rod placed in the vertical (*A*) and in the horizontal (*B*) position.

time he was surprised to find that his color vision had become normal. Examination confirmed that color vision was in fact normal. But his visual fields were still contracted. The abnormalities of sensory deviation had also disappeared, with the conspicuous exception that when horizontal and vertical lines were looked at with the right eye there was the same deviation as before. But when they were looked at with both eyes or with the left eye alone they were normal. Examination revealed disappearance of all disturbances of equilibrium. When the patient was reexamined two months later, perception with the right eye had become normal, too. On his last examination only pallor of both disks could be found. On the other hand, a new feature had appeared—disturbed stereognosis in his left hand.

The prominent feature of the disease was a systematized syndrome of disturbed equilibrium on the right. There was no proof of an actual space-occupying lesion.

With regard to these and other symptoms, a diagnosis of multiple sclerosis was considered, with chief localization of the lesions in the right cerebellar hemisphere. The remission and the course of the disease supported this diagnosis.

CASE 2.—*General Clinical Picture.*—R. F., a woman aged 35, had had transitory ataxia at the age of 15. She deviated to the right on walking, without ascertainable cause. In subsequent years she had had two attcks of "cute exhaustion," from which she recovered slowly. In addition, she had once had "some kind of paralysis" in her right arm, and, on advice of a neurologist, a lumbar puncture had been made. During the year prior to her admission the patient had felt a "paralysis" of sensibility in the right half of her body. The acute features of her illness, however, did not appear until the month preceding her admission. She noticed blurring of vision and unsteadiness of gait, especially in darkness. Since that time she had suffered from nausea, often followed by vomiting, and constant dizziness. The patient said she felt as dizzy as though she were sitting in a rocking boat.

On her admission to the hospital, examination revealed normal function of all cranial nerves, prompt reaction of the pupils to light and in convergence and unimpaired mobility of the eyes. The fundi, visual acuity and fields of vision were normal. Otologic examination showed normal hearing and normal vestibular reactions. Power, tone and active and passive movements of all extremities were normal. But there existed a slight diminution of superficial sensibility in all its qualities for touch, pain and temperature over the whole right side of the body. There were also a slight disturbance of the sense of position in her right hand and right foot and a certain slowness in otherwise normal stereognostic perception in her right hand. The sense of vibration was present on the right side of her body, but was somewhat diminished as compared with that on the left side. The reflexes showed no definite abnormality. Roentgenograms of the skull and examination of the blood and the cerebrospinal fluid revealed nothing significant. Examination showed additional disturbances of equilibrium and sensory functions, which will be described later.

Special Studies.—Disturbances of Body Posture and Equilibrium: The patient inclined her head to the right without knowing it. When her head was passively bent first to the left and then to the right and she was asked with her eyes shut to return it to the midline, she reverted to her primary position.

The patient used her arms without noticeable restriction. However, when she was asked with her eyes shut to keep her arms stretched out at the same level, it soon became evident that her right arm moved downward about 30 to 40 cm. and at the same time outward about 15 cm., while the left arm remained in its former position (fig. 6 *A*). Descent of the right arm was also observed when with her eyes shut the arms were stretched out sideways at the same level (fig. 6 *B*). When the patient with her eyes shut had one arm lifted to any given level and was then asked to lift her other arm to the same height, she always placed the right arm lower than the left. The patient was not aware of these deviations.

With her eyes open, the patient pointed equally well in any direction. With her eyes shut, however, she pointed accurately only with her left hand, while the right hand always deviated outward in a vertical plane and downward in a horizontal plane. When the patient with her eyes shut was asked to indicate a point in the midline of her body, she did so correctly with her left hand. With her right hand she always deviated outward about 5 cm. The amount of this outward deviation increased if the point to be indicated was lowered.

When the patient lying down with her eyes shut had both legs lifted to a certain level and was asked to keep them in this position, the right leg descended, unknown to the patient. When she was asked to lift her legs to the same level,

the right leg was always placed lower than the left. When the patient with her eyes shut had her left leg lifted passively and was then asked to lift the right leg to the same level, it was always placed lower to the same extent. At the same time, besides falling, the right leg also deviated outward. This outward deviation had already been noticed when she was performing the heel to knee test and the finger to nose test. When she was asked to touch with her right big toe the forefinger of the examiner placed exactly above it, her right leg always deviated outward. The deviation increased progressively as the test was repeated.

Even with her eyes open, the patient showed a slight inclination of the body to the right on standing; this inclination markedly increased when her eyes were shut, until a tendency to fall to the right resulted. When walking forward with her eyes open, the patient always deviated conspicuously to the right. This was

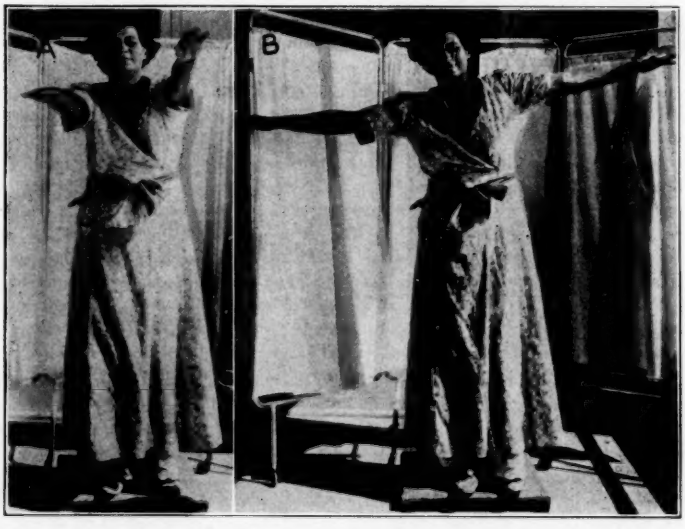

Fig. 6 (case 2).—Patient with arms outstretched, showing right arm lower than the left.

even more obvious with her eyes shut. When asked to move sideward with closed eyes, she deviated forward on going to the left and backward on going to the right.

Disturbances of Visual Perception: The patient reported that since the onset of her illness she saw everything as "unclear and faded." She was unable to define more accurately the disturbance, which varied greatly in intensity. She simply stated that her surroundings always "oscillated."

Examination revealed that she saw correctly with her left eye alone but that the right eye was affected. When she was allowed to look with her right eye alone, the sickroom appeared to her to be inclined about 25 degrees to the right, while the left side of the room seemed lifted and the right side lowered. This visual change of position occurred so suddenly and unexpectedly that the patient, for fear of falling out to the right, spontaneously clung to her bed. When

she shut her right eye and looked with her left eye alone, the room seemed normal again. When she looked with both eyes, the original visual impression of the room rocking from right to left returned, a phenomenon which can easily be explained by the different perception of the room by each eye.

Examination of the patient's visual perception by having her draw or recognize lines drawn by the examiner revealed further deviations when she looked with her right eye alone. When the patient was asked to draw a vertical line, she drew it with its lower end inclined to the right (fig. 7 *a*). A horizontal line she drew with its right end inclined downward (fig. 7 *b*). When the patient was shown truly vertical and horizontal lines, she saw them deviated as usual, the degree of deviation changing from 15 to 20 degrees in different examinations. The same deviation was also evident on her observing figures drawn by the

Fig. 7 (case 2).—Displacement of vertical (*a*) and horizontal (*b*) lines.

examiner. A right angle seemed to her to be an obtuse angle (fig. 8 *a*). A square seemed to be a rhombus, the vertical lines being inclined to the right and the horizontal lines inclined downward to the right (fig. 8 *b*). A circle seemed to her to be an ellipse, with its long diameter inclined downward to the right (fig. 8 *c*).

The handwriting of the patient showed no changes except for a pronounced deviation of the line of writing downward to the right.

Disturbances of Perception in Tactile and Haptic Spheres: When a small stick was placed first horizontally and then vertically on the patient's chest, it seemed to her to be horizontal and vertical only on the left side. On the right side it always seemed inclined. A stick placed truly vertically seemed to her to incline outward at its upper end and a stick placed truly horizontally seemed to incline upward at its right end.

When the patient with her eyes shut was given a rod to place vertically, she always placed it with its upper end inclined outward to the left (fig. 9 *A*). When she

was asked to do this with each hand separately, the inclination appeared only when she was using her right hand. When asked to place the rod horizontally, she always placed it with its right end inclined downward (fig. 9 *B*). The same deviation was observed on her doing the test with her right hand alone.

Impaired Estimation of Weight, Size and Distance: With her left hand the patient estimated weights very well. However, when in each hand there was placed a ball of wood of the same size and weight, the ball in her right hand always seemed lighter. Only after a weight of about 20 Gm. was added to the right ball or the same weight was taken away from the left one did they seem balanced.

The ball in her right hand seemed to be lighter, and also smaller than the one in her left. Thorough examination revealed that all objects put into her right hand, whatever the shape, seemed to the patient to be contracted in all

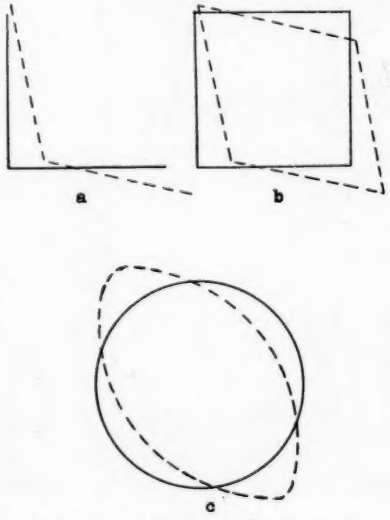

Fig. 8 (case 2).—Appearance of a square and a circle. As in figure 3, solid lines indicates the actual figure; broken lines, the subjective perception.

dimensions. The average difference was about 2 cm. for length and 1 cm. for thickness. The same underestimation was found when the patient was given small sticks of the same length between thumb and forefinger of each hand. Estimation of size and length of objects with the left hand was normal.

The same underestimation was found when she was asked to indicate with her eyes shut a certain point on a ruler with her forefinger. She did so correctly with her left hand; with her right hand, however, she always indicated a shorter distance, the average difference being 3 cm. independent of whether she was estimating in a horizontal or in a vertical plane, with each hand separately or with the two hands together.

Influence of Position of Head on the Pathologic Phenomena: As already mentioned, the patient inclined her head to the right without being aware of it. All the pathologic phenomena described were found and repeatedly confirmed

with the patient in this special position, whether she was standing, sitting or lying. One day, however, the patient changed her position, then inclining her head strikingly to the left. On being questioned cautiously, she stated that she inclined her head intentionally to the left because this position was most comfortable and gave her "relief." For the same reason, she also changed the whole position of her body, then lying slantwise in her bed and inclined to the left.

That this sensation of the patient as to the position of her head had a real somatic basis was shown by the following examinations:

When the examiner changed the position of the patient's head, a marked influence on the posture of the arms was seen. As already mentioned, when the

Fig. 9 (case 2).—Deviation of a rod placed vertically (*A*) and horizontally (*B*).

patient's head was inclined involuntarily to the right, the right arm was lowered at the same time, deviating outward without the patient's knowing it. When the examiner inclined or turned the patient's head to the extreme right, the speed and extent of falling almost doubled. When with both her arms stretched out the head was turned to the extreme left, the right arm was not lowered at all and remained in the same position as the left. Likewise, with the legs raised, the right leg was more quickly and powerfully lowered when the head was inclined to the extreme right, while it did not change its position when the head was turned to the extreme left.

The position of the patient's body, however, was not influenced by the position of the head. When her eyes were shut, she had a marked tendency to fall to the right. This tendency persisted with every position of the head and was not influenced by inclination to the extreme left. A change in the position of the head, to the left or to the right, did not influence past pointing beyond the midline.

Extreme inclination of the patient's head had also a marked influence on visual perception. When the head was inclined to the extreme right, the angle of visual deviation increased from 20 to 40 degrees, while it was reduced to about 10 degrees when the head was inclined to the extreme left. When the head was inclined to the extreme right, visual deviation was sufficient to affect the handwriting of the patient. As already mentioned, Latin script inclined downward to the right when seen with the right eye alone, while Hebrew script inclined upward to the

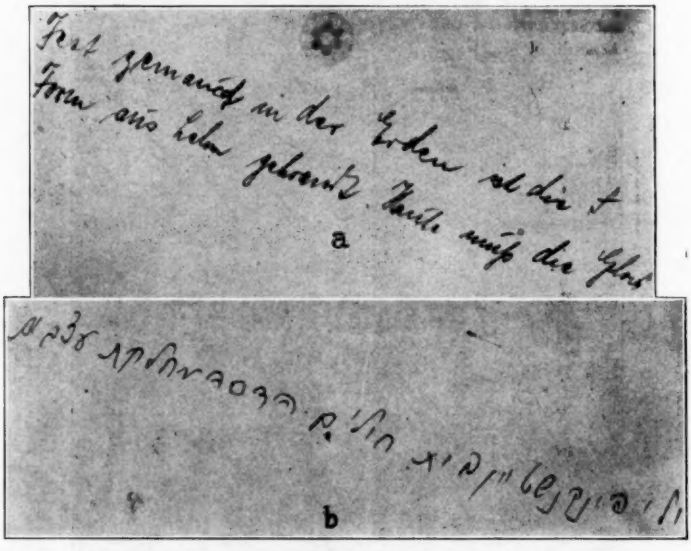

Fig. 10 (case 2).—Upward inclination of Hebrew script (*b*) and downward slant of Latin script (*a*) when the head was inclined extremely to the right.

left (fig. 10 *a* and *b*). This inclination to the same side ceased entirely when the head was inclined to the extreme left (fig. 11 *a* and *b*). With regard to the haptic sphere, the same increase in deviation of the horizontal and the vertical was obtained when the head was inclined to the extreme right, while reduction of deviation was observed when the head was inclined to the extreme left.

A change in the position of her head had also a pronounced effect on the defective estimation of weight, size and distance with her right hand. When the head was inclined to the extreme right, underrating increased considerably. Thus, when there was spontaneous inclination to the right, underrating of weight increased from 20 to 40 Gm., and underrating of size and distance, from 2 to about 4 cm. When, however, the head was inclined to the extreme left, estimation with the right hand became normal, and on testing there was almost no difference between the hands.

When sleeping, the patient involuntarily turned her head or body to the right. This change of position eventually influenced her dreams. When suddenly awakening from a dream of "flying," "falling" or "crashing down," she found herself nearly always lying on her right side.

Course of Disease.—During the following months the patient's condition gradually improved. The disturbances of equilibrium on the right side subsided almost completely, while the sensory phenomena diminished by degrees until they were no longer discernible. But the disturbance of superficial and deep sensibility persisted on the right side.

Diagnostically, the case could not be clarified entirely. There was no proof of a space-occupying lesion. The tendency to disturbed equilibrium on the right side had appeared apparently at an early age, while the disturbed sensibility probably appeared only in later years. Because of the remission of the chief disability, the diagnosis of a special form of multiple sclerosis with partial localization of the lesion in the right side of the cerebellum is possible, although not certain.

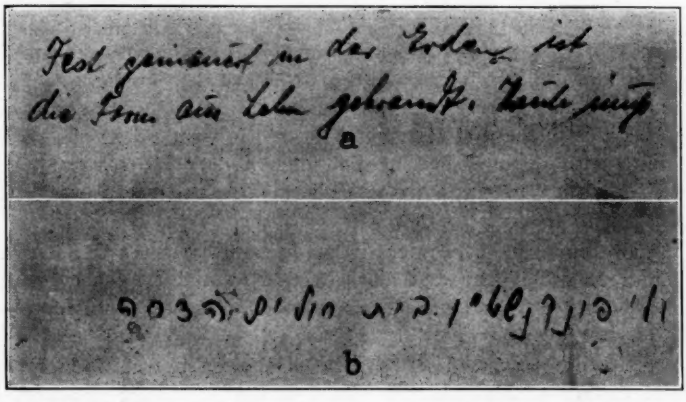

Fig. 11 (case 2).—Normal script (Hebrew and Latin) when the head was inclined to the extreme left.

Summary of Results.—The clinical picture established at the height of the disease in the 2 cases showed many strikingly similar disturbances in the motor, visual, tactile and haptic spheres. Disturbances in the motor sphere were concerned with the posture of the body, and in both cases systematized disturbance of equilibrium involving the right side was found. Directly connected with motor actions were the sensory functions of comparing weights placed in each hand; estimation of size as judged by feel in the hand or between thumb and forefinger, and estimation of distance. In the second case, all these features were greatly underestimated with the right hand. In view of well established experience in pure cerebellar syndromes, it is clear that this unilateral underrating of weight, size and distance is due solely to the basic disturbance of equilibrium and is not connected with the disturbance of sensibility on the same side. In support of this con-

clusion was the proved influence on underestimation of changing the position of the head and the total disappearance of these disturbances later, together with the other symptoms of disturbed equilibrium, although disturbance of sensibility still persisted.

With regard to vision, in both cases deviation in the perception of the coordinates of a room was found—in the first case when they were looked at with both eyes, in the second case when they were viewed wtih the right eye alone. Deviation of the coordinates also influenced the visual perception of geometric figures. In both cases deviation of the hand writing was found. Another visual disturbance was presented in the first case with dissolution of color perception. Of special interest was the fact that, in addition to normal vision for black and white, perception of red was intact. This proves that the dissolution was not due to atrophy of the optic nerve, as perception of red then disappears first, but was caused only by the basic disturbance.

In both cases the deviations in perception of the vertical and the horizontal was manifested also in the tactile and haptic spheres. In the second case the deviation in the tactile sphere was manifested not bilaterally, as in the first case, but only on the right side. The second case was also distinguished by the influence of the position of the head, inclination to the extreme right making the deviations worse, inclination to the extreme left improving them.

Finally, it must be mentioned that in both cases the deviation on the subject's walking forward and sideward showed a tendency similar to the deviation from the vertical and the horizontal found in other spheres.

Despite differences, the two patients showed the common fundamental quality of an inductive effect of the pathologic deviation in motor and other spheres, with essentially the same syndrome of systematized sensorimotor disturbances.

SYNDROME OF SENSORIMOTOR INDUCTION

The otologist von Urbantschitsch [1] has already referred to transitory disturbances in visual perception presenting themselves as illusory movements. His pupil Allers [2] made a further observation on disturbance of haptic perception in a blind man. But only Goldstein and Reichmann [3] and von Weizsäcker [4] recognized the basic relation of

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2. Allers, R.: Zur Pathologie des Tonuslabyrinthes, Monatsschr. f. Psychiat. u. Neurol. **26**:116, 1909.

3. Goldstein, K., and Reichmann, F.: Beiträge zur Kasuistik und Symptomatologie der Kleinhirnerkrankungen, Arch. f. Psychiat. **56**:466, 1915.

4. von Weizsäcker, V.: Ueber einige Täuschungen in der Raumwahrnehmung bei Erkrankungen des Vestibulärapparates, Deutsche Ztschr. f. Nervenh. **64**:1, 1919.

these sensory phenomena to motor functions. Günther,[5] Hoff and Schilder,[6] Wilder,[7] Ruffin,[8] Zingerle,[9] Halpern[10] and Quadfasel[11] published additional reports. However, the syndrome of sensorimotor induction can only be derived from those clinical observations the symptoms of which, like those in the present cases, indicate an inductive relation between sensory and motor functions.

REVIEW AND ANALYSIS OF CLINICAL FEATURES

The patient usually complains of persistent nausea, sometimes of vomiting and most of all of dizziness occurring spontaneously or after change in the position of the head, whereby dizziness can be increased or diminished. The patient often complains of his eyes swimming, of illusory movements of objects, of hazy vision and, in rare cases, of impaired perception of colors the nature of which cannot be explained by the usual ophthalmologic examination. If the patient reports that he sees objects distorted or has an unsteady gait in the dark, these clues should put the examiner on the right track and point to the appropriate tests.

In all the reported cases motor disturbances affected the equilibrium, and if lesions of other systems were not superimposed they appeared —provided that two foci were not present—in unilateral deviation of the limbs and of the whole body to the affected side (von Weizsäcker,[12] Goldstein,[13] Hoff and Schilder,[6] Zingerle,[9] Ruffin,[8] Halpern[10] and

5. Günther, K.: Ueber Vertikalempfindung, Ztschr. f. Ohrenh. **81**:345, 1921.

6. Hoff, H., and Schilder, P.: Zur Kenntnis der Symptomatologie vestibulärer Erkrankungen, Deutsche Ztschr. f. Nervenh. **102**:145, 1928.

7. Wilder, J.: Ueber Schief und Verkehrtsehen, Deutsche Ztschr. f. Nervenh. **104**:222, 1928.

8. Ruffin, H., and Stein, J.: Ueber den cerebralen Abbau von Sinnesleistungen, Deutsche Ztschr. f. Nervenh. **116**:56, 1930.

9. Zingerle, H.: Automatosesyndrom bei linksseitiger Stirnhirnerkrankung, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:249, 1933.

10. Halpern, L.: Ueber das Symptomenbild der Stirnhirnläsion unter spezieller Berücksichtigung der Störungen des Gleichgewichts, Monatsschr. f. Psychiat. u. Neurol. **94**:14, 1936.

11. Quadfasel, F. A.: Statische Haltungsstörung und intermodale Wahrnehmungsstörungen in ihrer gegenseitigen Abhängigkeit und Beeinflussbarkeit, Monatsschr. Psychiat. u. Neurol. **96**:326; **97**:90, 1936.

12. von Weizsäcker, V.: (*a*) Ueber eine systematische Raumsinnstörung, Deutsche Ztschr. f. Nervenh. **84**:179, 1924; (b) Kasuistische Beiträge zur Lehre vom Funktionswandel bei stato-opto-sensiblen Syndromen, Deutsche Ztschr. f. Nervenh. **117-119**: 716, 1931.

13. Goldstein, K.: Ueber induzierte Tonusveränderungen, Klin. Wchnschr. **7**:293, 1925.

Quadfasel[11]). In both my cases, with the syndrome of disturbed equilibrium on the right, the static and dynamic motor disturbances have already been described in detail. Only the posture of the head will be stressed. Secondary disturbances, caused by hydrodynamic, mechanical, meningeal or muscular irritative factors, will not be mentioned. Magnus,[14] in his classic experiments, discovered the neurobiologic importance of the posture of the head and its influence on muscular tone. The spontaneous inclination of the head in the present cases also indicates a primary disturbance of the equilibrium. Characteristically, the patient is unaware of this abnormal posture of the head, which manifests itself chiefly in a distinct inclination or turning of the head to the affected side (Goldstein,[13] von Weizsäcker,[12] Zingerle,[9] Halpern[10]). That this change in the posture of the head was subject to a certain law was proved not only on examination of perception of the vertical but also by the fact that the head of the patient when inclined by the examiner sometimes automatically returned to its primary position without the patient's being aware of it (Goldstein,[15] Halpern[10]). Sometimes, in the course of the disease, the patient instinctively changed his primary inclination to the affected side into an inclination to the normal side (Goldstein and Jablonski[16]). My second patient intentionally turned her head to the left from the position of spontaneous inclination to the right, as she noticed that this position made her feel more "comfortable." That this feeling is based on real causes and that the position of the head has central importance in this syndrome have already been shown in the studies on the same patient.

In the visual sphere the deviations in perception of coordinates and of geometric figures are of interest. These deviations manifested themselves either when the patient was seeing with both eyes, as in my first case, or when seeing with one eye alone, as in my second case (Weizsäcker,[17] Günther,[5] Goldstein,[13] Hoff and Schilder,[6] Ruffin,[8] Zingerle,[9] Halpern,[10] Quadfasel[11]). The extent of deviation varied from 5 to 20 degrees and was not always the same for the horizontal and for the vertical. Stable objects or drawings were perceived normally provided that the patient did not gage separate parts but perceived the object as a whole and the disturbances were only slight. That explains why patients in everyday life are not always aware of the character of their impairment.

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14. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

15. Goldstein, K.: Zum Problem der Tendenz zum ausgezeichneten Verhalten, Deutsche Ztschr. f. Nervenh. **109**:1, 1929.

16. Goldstein, K., and Jablonski, W.: Ueber den Einfluss des Tonus auf Refraktion und Sehleistungen, Arch. f. Ophth. **130**:395, 1933.

17. Weizsäcker, footnotes 4 and 12.

In addition to the constant disturbance in perception of coordinates, the patients sometimes have other disturbances in visual perception, the eyes otherwise being normal. Occasionally, they perceive a series of points as a continuous line, astigmatism being, of course, excluded (Goldstein,[8] Quadfasel[11]). In 2 cases there existed a micropsia, which in 1 case was restricted to one eye only (Weizsäcker[12b]), while in another case a macropsia was found (Goldstein and Jablonski[16]). In case of macropsia micrography developed, while in both my cases the handwriting deviated in direction. The disturbance of color perception found in my first case was remarkable. In 4 other cases there existed a dissolution of color perception of the degree of achromatopsia; the condition, however, like the micropsia found in my cases, was restricted to the eye on the affected side (Weizsäcker,[12b] Quadfasel[11]).

The fact that the deviation in perception of the horizontal and the vertical showed itself also in the tactile and the haptic sphere has been described in detail in this paper, as well as by Goldstein,[8] Weizsäcker[17] and Quadfasel.[11] Moreover, both my patients revealed the relation of tactile to visual deviation in that the first patient, with binocular deviation, had both sides of the body affected, while in the second, with only tactile and haptic deviation on the right side, visual deviation was restricted to that half of the body. The tendency of deviation may also affect the acoustic sphere in that a sound coming from the same distance to both ears was perceived by these patients as being displaced outward to one side (Goldstein,[18] Quadfasel,[11] Zingerle[9]).

Underestimation of weight in cases of unilateral cerebellar disturbances of equilibrium has long been known (Lotmar,[19] Maas,[20] Goldstein[21]). Besides unilateral underestimation of weight, unilateral underestimation of distance has also been observed (Goldstein and Reichmann[3]). In my second case, in addition to underestimation of weight and distance on the right side, underestimation of size of objects felt with the right hand was also found, while in another case there was overestimation of weight and size on one side (Zingerle[9]). In contrast the condition in both these cases, alternate overestimation and underestimation of size of objects felt with the hand was present in a third case (Allers[2]). This special disturbance in recognizing size by feel must be differentiated from the macro-

18. Goldstein, K.: Ueber induzierte Veränderungen des Tonus, Schweiz. Arch. f. Neurol. u. Psychiat. **17**:203, 1926.

19. Lotmar, F.: Ein Beitrag zur Pathologie des Kleinhirns, Monatsschr. f. Psychiat. **24**:217, 1908.

20. Maas, O.: Störung der Schwereempfindung bei Kleinhirnerkrankung, Neurol. Centralbl. **32**:405, 1913.

21. Goldstein, K.: Ueber Störungen der Schwereempfindung bei gleichseitiger Kleinhirnaffektion, Neurol. Centralbl. **32**:1082, 1913.

stereognosis manifesting itself in the course of restitution of cortical astereognosis (Halpern [22]), not only because of its different origin but also by the effect produced on it when the posture of the head is changed.

Systematic examinations in the motor sphere revealed that even as the position of the head is able to influence the position of the arms, so the position of the arms can automatically change that of the head. In addition, the position of the extremities can be influenced with reference to each other (Goldstein [23]). This mutual effect manifests itself also in the various sensory spheres. Thus, it was observed in a patient with left-sided disturbance of equilibrium with spontaneous deviation of the head to the right that his vision became worse when his head was turned to the left because of a change in refraction toward myopia (Goldstein and Jablonski [16]).

In my second patient inclination of the head from the right to the extreme left not only resulted in suspending the spontaneous lowering of the right arm but also improved and normalized the sensory achievements of visual, tactile and haptic perception and those of estimation of weight, distance and size, and even improved the deviation of handwriting. This effect can be obtained not only by changing the position of the head but also by changing that of the extremities. Thus, a series of points, which to a patient with spontaneous deviation of both arms to the left seemed to be a continuous line, were correctly recognized as such when he had his extremities turned to the right. Conversely, it became apparent that sensory functions influence the motor functions (Goldstein,[18] Zingerle,[9] Quadfasel [11]). Thus in these patients an isolated exposure of one eye to light resulted in a measurable increase of deviation of the arm on the same side. Indeed it became apparent that even different colors had a different effect on the posture of the arms, red increasing the tendency of deviation and green retarding it (Goldstein and Rosenthal [24]). In the acoustic sphere, also, a low sound increased the tendency of deviation, while a high one caused a slight lifting. In these patients there existed a mutual sensory effect. Thus, a vertical line which seemed to be inclined to the left, when looked at with the left eye was seen to be straighter after a tone was presented on the right side, whereas when a tone was presented on the left the inclination was still greater (Goldstein [18]). On the other hand, the observation that an isolated exposure of one eye to light caused the localization of a sound to the same side reveals the converse influence of an optic stimulus on

22. Halpern, L.: Macrostereognosia, J. Nerv. & Ment. Dis. **102**:260, 1945.

23. Goldstein, K.: Ueber induzierte Tonusveränderungen beim Menschen, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:383, 1924.

24. Goldstein, K., and Rosenthal, O.: Zum Problem der Wirkung der Farben auf den Organismus, Schweiz. Arch. f. Neurol. u. Psychiat. **26**:3, 1930.

acoustic perception. This tendency of mutual effect of sensory stimuli can be confirmed in the various sensory spheres.

In summary, the disturbances manifest themselves as follows: (1) disturbance of the motor function, resulting in unilateral deviation of the whole body and the separate limbs; (2) monocular and binocular deviation in perception of spatial structure, resulting in shifting of coordinates and geometric figures; (3) monocular and binocular micropsia and macropsia; (4) change in the size of handwriting and deviation of the line of writing; (5) monocular and binocular dissolution of color perception; (6) deviation in perception of vertical and horizontal coordinates in tactile and haptic localization; (7) one-sided deviation in acoustic perception; (8) change in perception of size of objects touched, resulting in unilateral microstereognosis or macrostereognosis; (9) unilateral underestimation of weight and distance, and (10) extensive mutual influence of motor and sensory functions.

These symptoms affect different functions and represent an unusual diversity of phenomena, at first sight seemingly unrelated. However, on thorough analysis exceeding the limits of the separate functional disturbances, they manifest common features of basic similarity. Thus, from the clinical point of view discrimination between primary and secondary symptoms seems indicated.

From this aspect, it is obvious that the phenomena of one-sided deviation manifesting themselves systematically in the motor, tactile haptic visual and acoustic spheres can be considered primary symptoms. These phenomena are the basic symptoms, because by their equal inductive effect they represent the characteristic features of this syndrome and are, in fact, its constant components, in contrast to the other, occasional symptoms. The clinical phenomena in themselves permit the conclusion of the one fundamental physiologic fact, that in some way the sensory perception of the external world is connected with the organization of the statokinetic system of the body. Normal statokinetic function is guaranteed by a steady perception of the horizontality of the ground plane and of the vertical planes passing symmetrically through the two halves of the body. In unilateral disturbance of equilibrium the statokinetic conditions are changed in such a way that the subjective midline of the body and the subjective horizontal plane are displaced. This displacement of the statokinetic system of the body then causes inductively a deviation in the sensory perception of the vertical and of the horizontal coordinates. Most interesting is the fact that the induced deviations appear not only in the haptic and tactile spheres, where effect depends on the active participation of the body, but also in the acoustic and visual spheres, which serve in perception of the external world independent of the activity of the body.

With regard to the basic fact of deviation, the inductive equality of the primary symptoms does not always presume equality as to the direction of deviation of the coordinates in the different spheres. Thus, when the spontaneous subjective phenomena of deviation are compared in my 2 cases, a different reaction can be seen. In my second case, for instance, the direction of deviation of the horizontal and the vertical coordinates were the same in the motor and in the sensory sphere. In my first case equal deviation of the vertical was also found. With respect to the horizontal, however, a different reaction could be stated, the deviations in the motor and in the visual sphere being equal in direction and deviations in the haptic and in the tactile being opposed. It must be noted that the reaction of the outstretched arms, which I suppose to indicate the subjective horizontal of the body, did not result in this case in a dropping of the outstretched arm, but on the contrary, in lifting it. Thus the question arises whether lifting of the arm, instead of dropping it, was not in this case the result of a compensatory phenomenon, like that of turning the head from the affected to the normal side. This view seems to be more probable in that this reaction is contrary to the pathologic tendency and occurred without the patient's being aware of it. Thus, this occurrence can be looked on as being a biologic regulation to render the organism more efficient under the prevailing pathologic conditions.

These primary symptoms of inductive sensorimotor deviation being clinically well founded, the special circumstances in which they appear and the underlying physiopathologic mechanisms are not yet established. Goldstein [18] stated the belief that these phenomena are a confirmation of his conception of the influence of motor proceedings on the structure of our perception. He points out that each action of the organism is connected with a tendency of the whole organism "toward the stimulus." This fundamental biologic phenomenon manifests itself, for instance, in the primitive world in the turning of a leaf toward light and appears in man only under pathologic conditions. The results, previously described, of unilateral change in motor functions in its inductive effect on the optic, tactile and other sensory spheres confirm the validity of this biologic rule as regards man and reveal, in addition, the importance of kinetic proceedings, especially on the structure of one's spatial perception.

From the physiologic point of view, the symptom of an extended mutual effect of motor and sensory proceedings may be thought of as a link between the primary and the secondary symptoms. It not only explains the possibility of an inductive accomplishment of the primary sensorimotor symptoms of deviation but helps also the understanding of the secondary symptoms. These include, first, the visual symptoms of micropsia and macropsia and the dissolution of color perception,

while micrography is caused by macropsia and the deviation of the line of writing is due to the tendency to deviation. Other secondary symptoms are altered perception of weight, distance and size when the object is touched with the hand. As may be seen, all these inconstant secondary symptoms affect solely the functions of sensory perception. One must assume that weakened statokinetic stability, which causes the primary syndrome of deviation, affects all other action of the various sensory organs. The sensory organ suffers from an altered threshold of perception, which results in an abnormal realization of the stimulus. This alteration may consist of a coarsened differentiation and dissolution of sensory perception as to quality. In the optic sphere, blurred differentiation caused by coarsening of the threshold of the stimulus manifests itself, for instance, in resolving a line of dots into a continuous line, a manifestation corresponding to the coarsening of spatial discrimination of two points in the sphere of sensibility. Dissolution of color perception, occurring generally in one eye, may also be included here. The fact that in a colortop with black and white sectors the blending to gray appears more quickly in the affected than in the normal eye leads to the belief that in this instance also altered differentiation of color perception is due to coarsening of the threshold of the stimulus. In the central projection of the coarsened sensory stimulus the altered duration of the course of nervous excitation is certainly also very important, as the phenomenon of delayed reaction to pain in the sphere of sensibility proves quite obviously. Of essential importance is the fact that, perception and projection being altered, the sensory effect produced by the stimulus can also assume a change as to its quantity. In the sphere of sensibility this fact manifests itself in the phenomenon of abnormal irradiation of a local stimulus of pain associated with thalamic lesions and in the protopathic phase of the regeneration of a peripheral nerve. In the sensory sphere a changed perception as to quantity appears in the phenomenon of macrostereognosis following recovery from astereognosis. These observations may serve to explain the analogous phenomena of the sensory effect of irritation in the clinical picture of sensorimotor induction. The altered perception as to quantity of visual impressions, and of weight, distance and size—the affected systems even differing—derives from the same mechanism of the pathologically changed perception and projection. Of real importance is the fact that these phenomena also occur in disturbed equilibrium. and then are induced by motor proceedings.

LOCALIZATION OF THE SYNDROME

The question of the localization of this syndrome is, of course, most interesting. Reasoning from the almost bewildering abundance of different symptoms, van Weizsäcker [12] initially assumed a "metaorganic

area of function." The distinction previously made between primary basic symptoms and inconstant secondary symptoms may be of value in that the problem of localization is restricted and dervied only from the primary sensorimotor symptoms of deviation. The fact that the one-sided systematic disturbance of equilibrium is decisive and obligatory for the origin of the primary symptoms and for the whole syndrome attracts one's attention chiefly to the areas of regulation of the equilibrium with regard to localization.

The question of a vestibular localization will be discussed first. The relevant cases hitherto described reveal that an exclusively vestibular localization is almost out of the question. In the first case of von Weizsäcker [4] and in the case described by Hoff and Schilder,[6] in which a difference in vestibular irritation appeared, there existed also obvious disturbances of the equilibrium which indicated decisively a lesion of the cerebellum. On the other hand, in none of the other cases of disturbed sensorimotor induction were either subjective or objective vestibular disturbances shown. Therefore the localization of the existing syndrome must be placed in the supravestibular areas of regulation of the equilibrium.

Thus, one is entitled to assume in this instance a cerebellar localization which is indicated by the mere clinical symptoms alone. Two anatomically verified cases established this view. In the case of Günther,[5] with unilateral disturbed equilibrium and phenomena of deviation in the optic and haptic spheres appearing before death, an abscess in the right cerebellar hemisphere was found. Still more convincing than this case, in which the abscess originated from the ear and a lesion of the homolateral vestibular organ could be assumed, is a case reported by von Weizsäcker.[12b] Besides disturbed equilibrium on the left side, there existed phenomena of deviation in the visual sphere. Autopsy revealed an arteriosclerotic softening in the left cerebellar hemisphere. Goldstein,[13] on the other hand, was the first to show that sensorimotor phenomena occur not only in patients with cerebellar lesions but also in patients with frontal lesions. Zingerle [9] described right-sided sensorimotor phenomena in a patient with a lesion in the left frontal area which was found at biopsy. Trephination showed circumscribed meningitis in the left frontal lobe. After recovery all disturbances gradually subsided. Halpern,[10] too, reported a case with a lesion in the left frontal lobe. This patient presented a syndrome of disturbance in equilibrium on the right side and deviation in perception of the coordinates of the room on the same side. In this case the projection of the lesion in the skull corresponded to the area of the second and third convolutions of the frontal lobe. Thus, these findings confirm anatomically the central localization of the syndrome in the cerebellum and the frontal

lobe, with the difference that the syndrome usually manifests itself homolaterally with cerebellar lesions and contralaterally in patients with frontal lesions.

The localizing relation of unilateral disturbances of the equilibrium to certain parts of the contralateral frontal lobe is already known. The occurrence of the syndrome of sensorimotor induction with lesions of the cerebellum as well as with lesions of the frontal lobe also confirms the connection of the central regulation of equilibrium to the fronto-cerebellar system with regard to function and localization. The function of the vestibular apparatus with respect to regulation of equilibrium must be regarded as that of a peripheral organ in relation to its centers. In this connection the anatomic findings are worth mentioning, revealing that the fibers of the vestibular organ extend into the paleocerebellum, while the frontal fiber tracts radiate into the neocerebellum, namely, the cerebellar hemispheres. It thus results, the whole system of equilibrial regulation being uniform in function, that a difference in structure between the peripheral vestibular organ and the paleocerebellum, on the one hand, and the neocerebellum and the frontocerebellar system, on the other, must be assumed. From the point of view of an anatomic differentiation of the peripheral and the central part of the equilibrial system, the basic difference in the symptoms of peripherally and of centrally disturbed optical perception of the external room will again be briefly stressed. The condition of dizziness, as caused by the peripheral vestibular organ, is usually of circular nature and occurs in a "round room." It is accompanied above all with the patient's feeling that his body is being moved in the external room or that the room is moved around him, as a result of which the synergism of his movements is disturbed to such a degree that it becomes almost impossible to keep the body upright. In contrast to this prevailing "subjective" quality of pathologic perception of the external room, the disturbed perception of central origin is not connected with the "ego" and is objectively stated to be a constant alteration of the stable external room with respect to one or several coordinates. This optical deviation of central origin in the perception of the external world as a separate symptom of a much more extensive syndrome has already been discussed.

GENERAL ASPECTS

The phenomena described here are unusual with respect to their abundance and character. The attempt at a clinical differentiation between the constant sensorimotor primary symptoms and the inconstant sensory secondary symptoms has perhaps served to render these phenomena more understandable. Nevertheless, many features cannot as yet be explained from the physiopathologic standpoint. However, the clinical facts established are sufficient to disclose new aspects.

These facts enrich the neurologist's method of clinical examination and knowledge of symptoms, which until now were unknown or, rather, unobserved. They show, furthermore, that the clinical picture of disturbed equilibrium exceeds greatly the merely motor disturbances of posture and may even produce systematized disturbances of various sensory functions. They reveal, in addition, that the usual ophthalmologic examinations of refraction, eyegrounds, visual fields and acuity of vision are no longer sufficient to check all functions of the eye, but that examination of the visual perception of the external room must be included. Thus, the organic nature of many a patient's complaints, having been dismissed as "nervous" or "hysterical," will be recognized.

In addition to the clinical aspect, the phenomena described disclose other new points of view. It follows that every symptom is not necessarily related to the anatomic lesion, but that many are simply the manifestations of altered function. The concept, long forming, of the essential importance of the functional disturbances, instead of the far too prevalent anatomic orientation, is thus confirmed from this point of view. Of basic importance also is the intelligence gained on the deciding influence of motor proceedings on sensory perception n general, especially on the structure of spatial perception. The perception of the external room being normally based on the optical function, the pathologic phenomena described reveal, however, that this optical foundation depends essentially on statokinetic conditions. Furthermore, proofs exist that many reported spatial visual hallucinations actually belong to the sphere of the organically disturbed perception of the external room. Finally, in the light of the described facts of a mutual influence of the sensory functions on one another, the psychologic theory of the synesthesias acquires a new physiologic aspect.

The aspects suggested require, of course, further confirmations. Here, as in many other spheres of neurologic research, such as the aphasic, apratic and gnostic disturbances, only the afflicted human being can serve as the source of knowledge.

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Case Reports

CEREBRAL FAT EMBOLISM

Report of a Case with Recovery

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Recovery from cerebral fat embolism is exceedingly rare. In this report we record the complete recovery of a patient with cerebral fat embolism and comment briefly on the literature.

REPORT OF CASE

J. T., a 20 year old athlete, sustained a fracture of the right tibia and fibula playing football on Nov. 2, 1947. There was no other injury, and he was fully conscious. Splints and traction were applied before he was taken to the Cape Cod Hospital, at 3:35 p. m. Roentgenograms taken at once without disturbing the splints revealed oblique fractures of both bones just above the midpoint with some posterior displacement of both lower fragments. Position was satisfactory enough to warrant application of plaster to the midthigh; the patient was given morphine sulfate, ¼ grain (15 mg.) and put to bed. No manipulation or reduction was done and no anesthesia given.

Physical examination at that time showed a healthy, well developed, young man. He was alert, with moderate pain in the injured leg, and was clear and well oriented. Heart, lungs and results of neurologic examination were normal. He had an uneventful night and went to the roentgenology department at 10:30 a. m. for recheck, which showed no change in the position of the bones.

At 11:30 a. m. he could not be aroused, and twenty minutes later he was incontinent, broke out in a sweat, had a chill and was cyanotic; the pupils were pinpoint, and there was nystagmus. The temperature was 101 F., the blood pressure 140 systolic and 50 diastolic, and the respiratory rate 40. The leukocytes numbered 21,000, with 82 per cent polymorphonuclear cells, and the urine contained albumin. A roentgenogram of the chest showed normal conditions. Lumbar puncture at 9 p. m. yielded clear fluid under normal pressure, containing no cells and a total protein concentration of 28 mg. per hundred cubic centimeters.

Fat embolism was suspected, and ligation of the right femoral vein was done at 11 p. m. (by Dr. John O. Niles). The patient remained delirious and in a semicoma all night. In the morning he had petechial spots all over the chest, abdomen, arms, shoulders and face. He was seen at this time by the neurologic consultant (R. S. S.), who found a drowsy but arousable patient who could talk. The neck was not stiff; the pupils reacted to light, and the fundi were normal. Corneal reflexes were present. The nystagmus had disappeared. There was weakness of the lower portion of the left side of the face, with increased reflexes on the left side and a positive Babinski sign. Transfer to the Massachusetts General Hospital was advised and completed by afternoon. On arrival there, the patient showed essentially the same picture as at the Cape Cod

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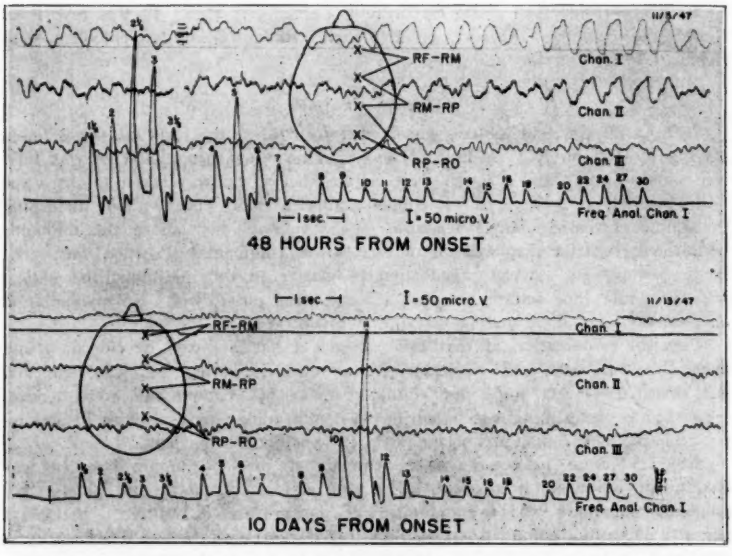
Hospital, except that in the fundus of the right eye there was a very small pale spot below the disk. A biopsy specimen taken from the skin of the petechial area showed an increased amount of fat. Blood fat was 285 mg. per hundred cubic centimeters, which is normal, and there was no fat in the urine. The electroencephalogram showed diffuse 3 cycle high voltage slow waves on both sides, most marked in the posterior frontal area on the right side (the chart).

The patient began to improve steadily and became clear, alert and oriented on the fifth day after the embolism. The left-sided signs disappeared on the sixth day, and the electroencephalogram was within normal limits on the eighth day (the chart). Intelligence tests showed no defects and normal intelligence quotient. The patient was afebrile and free from pain and complaints of any



Electroencephalogram in cerebral fat embolism. The upper half of the chart shows four points on the right side of the head from which the electroencephalogram was taken forty-eight hours after the onset of the embolus. The tracing on the left side was essentially similar but not so marked. The tracing has on it the automatic frequency analysis of the waves coming from the frontal to postfrontal leads, shown in the fourth line, indicating that most of the activity is in the 2, 2½ and 3 per second band with a secondary peak in the 5 per second band and no activity in the normal alpha or beta group. The bottom part of the chart shows the same electrode placements ten days from the onset, when clinical recovery was complete. The frequency analysis of the tracing from the frontal to the postfrontal leads is again indicated on the bottom line and indicates no activity in the delta or slow-band and none in the intermediate slow band around 5 per second, a peak in the normal 11 per second alpha band and no other activity. Calibration and time scale are shown between the two records.

kind and was discharged home on the tenth day after the embolism. Subsequent follow-up of this patient five months later showed a normal neurologic status, mental status, laboratory findings and electroencephalogram.

COMMENT

There is an extensive literature and a good deal of experimental work on fat embolism. The classic paper covering the general problem in most detail is that by Killian,[1] published in 1930, in which the author stated that the problem is eminently a German one, since most of the literature is in that language. He listed over 200 references and stated that the incidence of fat emboli in cases of fracture is less than 0.3 per cent and in the fatal cases evidence of fat in the brain is found histologically in one third of the cases. There are numerous interesting case histories and very definite data to show this phenomenon occurs in the absence of a patent foramen ovale. Blood fat may be normal, and the urine may be free of fat.

In 1933 Strauss [2] published a review of the cases with involvement of the central nervous system. In 124 such cases, he found 103 in which the embolus resulted from fractures, 84 of which were in the lower limb. Eighty-five per cent of the patients died, and the spinal fluid was usually normal. Strauss emphasized the fact that in over two thirds of the cases the symptoms occurred within twenty-four hours of the fracture and 80 per cent of the deaths occurred two days after onset of the embolic phenomena. He mentioned that diagnosis can be made from the period of twelve to twenty-four hours after fracture in which there is freedom from symptoms and signs, sudden onset of pulmonary and cerebral signs and petechiae in the skin, mucous membranes, conjunctivas or eyegrounds.

Two fatal cases with cerebral involvement were reported by McCarter [3] in 1937; pathologic data are included in the report.

In 1939 Harris, Perret and MacLachlin [4] reported 2 fatal cases and 6 cases with recovery, and in the same year Whitaker [5] reported 2 cases with recovery

The finding in this patient of abnormal electroencephalographic waves shortly after the embolism occurred suggests that it might be desirable to investigate with the electroencephalograph the problem of mild embolic phenomena due to fat in a routine examination of patients who have sustained a fracture. The test is, of course, very simple to apply and would indicate the presence of mild degrees of cerebral involvement. It is well known that many patients with fracture are restless or irritable or complain of headaches or are nauseated during the first or second twenty-four hour period after the injury. This has been attributed to the effect of anesthesia, traumatic shock, emotional difficulties or the effects of medication. It is hoped that this communication will stimulate future investigation along these lines.

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FATAL AGRANULOCYTOSIS DUE TO TRIMETHADIONE (TRIDIONE®)

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NEW YORK

THE WIDE use of trimethadione (3, 5, 5-trimethyloxazolidine-2, 4-dione, tridione,® Abbott) for the control of petit mal and of psychomotor seizures compels the careful evaluation of toxic effects of the drug and comparison of these effects with the results to be achieved by its use. In 1946 DeJong [1] reported that no serious reactions to trimethadione had yet been observed and that the only untoward effects noted were nausea, drowsiness and lightheadedness. Later in the same year Harrison, Johnson and Ayer [2] reported a case of fatal aplastic anemia following the simultaneous use of trimethadione and a hydantoin. Mackay and Gottstein [3] reported a case of their own of fatal agranulocytosis and aplastic anemia attributable solely to trimethadione, and Greaves [4] reported a case of agranulocytosis with recovery in a patient who had also been receiving the drug. In 1948, Carnicelli and Tedeschi [5] added a fourth case of bone marrow depression with trimethadione, again with fatal outcome despite withdrawal of the drug and vigorous therapy. All 3 fatal cases were marked by progressive deterioration of the bone marrow. In this report we wish to record a similar experience.

REPORT OF CASE

S. W., a 37 year old woman, had suffered from frequent attacks of petit mal since the age of 9 years. She was treated with phenobarbital irregularly and with only moderate success until 1939, when therapy with diphenylhydantoin sodium was instituted. There was marked diminution then in the frequency of the seizures. Two months prior to her admission to the Bronx Hospital this therapy was discontinued and the patient was given trimethadione, 0.3 Gm. thrice daily. No other medication was taken during the period of trimethadione therapy. The petit mal seizures remained under control, and therapy was continued. Blood counts at irregular, widely spaced intervals were normal until nine days prior to admission, when the leukocyte count was found to be 1,200 cells per cubic milli-

From the Departments of Medicine and Pathology of the Bronx Hospital and the Office of the New York City Medical Examiner.

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3. Mackay, R. P., and Gottstein, W. K.: Aplastic Anemia and Agranulocytosis Following Tridione, J. A. M. A. **132**:13 (Sept. 7) 1946.

4. Greaves, R. J.: Correspondence, J. A. M. A. **132**:44 (Sept. 7) 1946.

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meter, with 25 per cent segmented forms (granulocytes). The patient was asymptomatic at this time. Use of trimethadione was halted, and penicillin was administered orally by her physician. Two days prior to admission the leukocyte count was 2,000 with 17 per cent granulocytes, of which 6 per cent were eosinophils. The patient was still asymptomatic when this count was taken, but on the following day cellulitis of the back of the neck and right thigh developed and the temperature rose to 104 F. She was admitted to the Bronx Hospital within twenty-four hours of the onset of symptoms, on Aug. 3, 1948.

On admission the patient was acutely ill. Significant physical findings were confined to the areas of cellulitis mentioned. On the back of the neck there was an irregular, 8 by 4 cm. area of redness and induration without fluctuation. There was a similar but smaller area on the right thigh.

Therapy was instituted, consisting of application of wet dressings locally and administration of 100,000 units of penicillin every three hours intramuscularly. On the third day the dose of penicillin was increased to 100,000 units every two hours. On the sixth day streptomycin, 3 Gm. daily, and pentnucleotide,® 10 cc. intramuscularly twice daily, were administered. Large doses of vitamin C were

Differential Leukocyte Counts

Hospital Day	Hemoglobin, Gm.	Leukocytes, No.	Polymorphonuclears, %	Eosinophils, %	Lymphocytes, %	Monocytes, %	Platelets, No.
1	14	1,300	29	0	58	13	130,000
2	..	1,000	22	4	60	14	.....
3	..	900	8	0	78	14	.....
4	..	1,400	0	4	92	4	.....
5	..	750	4	0	96	0	.....
6	14.5	700	0	0	90	10	.....
8	..	950	0	0	92	8	.....
9	..	700	0	0	94	6	.....
10	..	400	0	0	98	2	.....

given, and the patient received seven transfusions during her eleven day stay in the hospital. Four of these transfusions consisted of freshly drawn blood.

On this regimen the areas of cellulitis diminished in size but central areas of necrosis developed. There was no evidence of pus formation at any time. On the fifth day petechial and purpuric eruptions developed over the trunk and extremities, together with menorrhagia which persisted to the time of her death. The temperature course was irregular, with a steady tendency to rise. It reached a maximum of 106 F. on the sixth and again on the tenth hospital day. On the tenth day the patient became stuporous and rhonchi through both lung fields with cough and expectoration of large quantities of frothy, mucinous material developed. She died twenty-four hours later.

At the time of her admission her hemoglobin level, red blood cell count and platelet count were normal; the only abnormalities noted were in the white blood cells. There were no band forms at any time, and other granulocytes disappeared entirely from the differential count after the fifth hospital day (the table).

Sternal marrow aspirated on the second day revealed a severe depression of all myeloid elements, with a total count of only 10,400 cells per cubic millimeter. The myeloid series made up only 5.5 per cent of all nucleated cells present, and these were all eosinophils. There was no abnormality of the erythroid series. However, there were less than 10 megakaryocytes per cubic millimeter, despite the absence of depression of platelets in the peripheral blood. The bleeding and coagulation times were normal, and several blood cultures were sterile.

The necropsy was performed by one of us (I. M.). Bilateral pulmonary congestion and edema were noted. Hemorrhages, mostly petechial in size, were found throughout the small and large bowel, in the kidneys and urinary bladder and in the uterus. Both adrenal glands were extensively hemorrhagic. Interstitial hemorrhages were found in the adventitia of the aorta. The cutaneous lesions that had been present on admission were ulcerated and necrotic. No evidence of suppuration was found anywhere.

Bone marrow taken from the vertebrae and ribs at necropsy confirmed the antemortem observations. There was a great decrease in the cellular elements, and all cells present were of the erythroid series.

Sections of the brain revealed no lesion that could be held responsible for the patient's seizures.

COMMENT

Trimethadione is generally conceded to be ineffective in grand mal and of value essentially for petit mal and psychomotor seizures.[1] Its use in these conditions is certainly widespread; the appreciation of its potential toxic effects is perhaps less so. It has been pointed out[3] that the molecules of trimethadione and aminopyrine both contain a pentagonal ring with a carbonyl group similarly placed. That the latter drug causes agranulocytosis is commonly known. In the light of this and similar reports, the need for careful clinical and laboratory control of patients receiving trimethadione is obvious.

SUMMARY

A case of agranulocytosis with fatal outcome due to trimethadione is reported. Similar case reports in the literature are referred to. These indicate that proper precautions should be taken with patients receiving trimethadione therapy.

Drs. Gamliel Saland and I. Rothstein assisted in this study.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

THE HISTOLOGICAL PATTERN OF METAMERIC DEVELOPMENT IN ARTEMIA SALINA. PAUL B. WEISZ, J. Morphol. **81**:45 (July) 1947.

Weisz describes the larval history of the brine shrimp (Artemia salina) strictly from the point of view of metameric development.

The manner in which a continuous over-all pattern of metameric development, precisely defined in relative time and space, governs the histologic sequences may be illustrated by the formation of the nervous system. The appearance and maturation of solid ingrowths from the ventral ectoderm are geared to the segmental development. Within two stages after a given thoracic segment is externally visible, the earliest ganglionic anlage is formed. After an interval of three stages, the anlage assumes mature ganglionic characteristics and connects by axon fibers with parts of the nerve trunk immediately anterior. At this time the segmental musculature is laid down in myoblast form, and the appendage performs noncoordinated, jerky movements. Since through three stages a ganglion is present only in rudimentary form, there are three successive segments in the thorax, through most of the larval period, in which ganglia are just in the process of being formed; every more anterior segment has a pair of mature ganglia, while more posteriorly no nerve material is present at all.

The anterior segments of the head are not segmentally divided. Nevertheless, a definite pattern of head segmentation emerges when the time sequence of clearly observable phenomena, viz., nervous and appendageal development of posterior head segments, is provisionally applied to all head segments; isolated bits of evidence concerning anterior segments then fall into place, and the pattern assumes a plausible degree of reality.

As a result of the analysis of the histologic pattern, Weisz finds that a fundamental relation exists between a given cell mass and the course of possible differentiation. This is shown in the development of thoracic appendages, in which the ratio of ectodermal to mesodermal mass at a critical time determines what type of appendage can form. It is in this way that, in spite of serial homology, there is obtained an absence of serial analogy. REID, New Brunswick, N. J.

A QUANTITATIVE STUDY OF LOCOMOTION IN LARVAL AMBLYSTOMA FOLLOWING EITHER MIDBRAIN OR FOREBRAIN EXCISION. S. R. DETWILER, J. Exper. Zool. **102**:321 (Aug.) 1946.

The locomotor responses of larvae lacking the cerebral hemispheres and the dorsal portion of the diencephalon were compared with those of larvae in which the midbrain was replaced by the anterior end of the spinal cord. A special device made possible the quantitation of the swimming responses to twenty-five successive stimulations. Young larvae lacking the midbrain were found to do as well as control larvae up to about stage 40 to 41. The subsequent decrease in responses to tactile stimulation and the striking failure in locomotor capacity may be

regarded as due to the absence of the tectobulbar and tectospinal tracts, which normally dominate the previously autonomous spinal mechanism.

While the swimming scores of larvae lacking the cerebral hemispheres are somewhat lower than those of normal controls of the same stage (apparent after stage 40 to 41), their motor ability and response to tactile stimulation are maintained. This status is in striking contrast to the decline in motor ability exhibited by animals lacking the midbrain. The data presented indicate the relative unimportance of the hemispheres in the general motor activity of the larvae. The device used in these studies for quantitating the motor ability is being applied to further behavior studies.

REID, New Brunswick, N. J.

THE NERVOUS SYSTEM AND REGENERATION OF THE FORELIMB OF ADULT TRITURUS: VI. A FURTHER STUDY OF THE IMPORTANCE OF NERVE NUMBER, INCLUDING QUANTITATIVE MEASUREMENTS OF LIMB INNERVATION. MARCUS SINGER, J. Exper. Zool. **104**:223 (March) 1947.

Singer reports an analysis of the influence of the number of nerve fibers on regeneration in the midforearm, the hand and the digits (2, 3 and 4) of the newt, Triturus viridescens. As in the upper arm, definite quantitative requirements must be met for regeneration to occur. The results show a threshold range above which regeneration always occurs, below which it is invariably absent and within which regeneration usually occurs.

The quantity of fibers required for regeneration at each level of the limb varies, being lowest in the digits and highest in the forearm. The midforearm level has a threshold similar to or higher than that of the upper arm. The quantity of nerve fibers required by each of the digits depends on the relative size of the digit, being largest for digit 3. As a result of this analysis, Singer advances the theory that the number of fibers required at the cut surface is, in part at least, a function of the quantity of tissue subjected to the regeneration process, which can be expressed in terms of the area of the amputation surface.

In addition to the experimental data, the normal counts for each of the spinal nerves (3, 4 and 5) at each of the experimental levels (midforearm, hand and digits) are presented.

REID, New Brunswick, N. J.

Physiology and Biochemistry

THE ACUTE EFFECTS ON THE CEREBRAL CIRCULATION OF THE REDUCTION OF INCREASED INTRACRANIAL PRESSURE BY MEANS OF INTRAVENOUS GLUCOSE OR VENTRICULAR DRAINAGE. HENRY A. SHENKIN, EUGENE B. SPITZ, FRANCIS C. GRANT and SEYMOUR S. KETY, J. Neurosurg. **5**:466 (Sept.) 1948.

Previous investigation by two of the authors (Kety and Shenkin) indicated that a rise in intracranial pressure produced by a brain tumor was associated with an increase in the cerebrovascular resistance, an increase in the mean arterial blood pressure and, if the intracranial pressure was high enough, a decrease in the cerebral blood flow. With this in mind, Shenkin and associates attempted to determine what changes took place in these functions by decreasing the intracranial pressure through the intravenous administration of dextrose or by direct ventricular drainage. Twelve patients were used—6 were given dextrose (150 cc. of a 50 per cent solution) intravenously and 6 had ventricular taps only. The subjects whose ventricles were tapped failed to show any significant change in cerebral blood flow, cerebral metabolism, mean arterial blood pressure or cerebro-

vascular resistance, even though the pressure was reduced to normal by the tap. In the 6 patients receiving dextrose there was an increase in the cerebral blood flow, with no change in the cerebral oxygen consumption or in the mean arterial blood pressure. The cerebral vascular resistance was appreciably decreased. The decrease in the actual intracranial pressure of the patients treated with dextose was not as great as that in the patients treated by ventricular drainage.

The authors conclude from this study that it is probably the hemoconcentration of the blood by the hypertonic solution of dextrose that increases the cerebral blood flow and lowers the cerebrovascular resistance. There was no significant change in the oxygen delivered to the brain after injection of dextrose, but metabolic products, not dependent on hemoglobin transport, may be removed from the brain by the increased cerebral blood flow.

No studies after repeated use of these methods for reducing intracranial pressure were reported.

TOZER, Philadelphia.

SYNAPTIC CONDUCTION TO GIANT FIBERS OF THE COCKROACH AND THE ACTION OF ANTICHOLINESTEROSES. KENNETH D. ROEDER, NANCY K. KENNEDY and EVELYN SAMSON, J. Neurophysiol. **10**:1 (Jan.) 1947.

Roeder, Kennedy and Samson point out that insects offer especially good opportunities for studying nerve conduction mechanisms, since the neurons are proportionately larger and the nervous system is divided into discrete ganglia. In the cockroach a large number of sensory fibers enter the sixth abdominal ganglia, forming synaptic connections with twelve to sixteen giant fibers. These synapses conduct synchronously up to 400 stimuli per second, with a delay of 0.6 to 1.5 milliseconds. Treatment with diisopropyl fluorophosphate (DFP) produces marked synaptic facilitation alternating with periods of synaptic block, even after washing in saline solution. The conduction process, however, in the giant fibers is unaffected by diisopropyl fluorophosphate. The authors conclude that transsynaptic conduction is dependent on cholinesterase. Acetylcholine alone has no effect on such conduction, but in the presence of diisopropyl fluorophosphate acetylcholine blocks the conduction across synapses. Physostigmine, neostigmine and strychnine block transsynaptic conduction and fail to sensitize the ganglion to the blocking action of acetylcholine.

FORSTER, Philadelphia.

GENERALITY OF THE ROLE OF ACETYLCHOLINE IN NERVE AND MUSCLE CONDUCTION. T. H. BULLOCK, H. GRUNDFEST, D. NACHMANSOHN and M. A. ROTHENBERG, J. Neurophysiol. **10**:11 (Jan.) 1947.

The authors employed two approaches in studying the generality of an essential role of acetylcholine in the conduction of nerve and muscle. One method was based on the effect of cholinesterase inhibitors on the action potential of various kinds of nerves and muscles; the other method was evidence for the presence of the specific cholinesterase. Di-isopropyl fluorophosphate (DFP) abolishes reversibly the action potentials of sensory and motor nerves. Physostigmine abolishes the action potential of adrenergic nerves. The action potential of curarized frog muscle is abolished by di-isopropyl fluorophosphate and by physotigmine. In both sensory and motor nerves cholinesterase is present in a significant concentration, and in adrenergic nerves, in a high concentration. From this evidence, Bullock, Grundfest, Nachmansohn and Rothenberg conclude that the role of acetylcholine in the conduction of impulses is a general one.

FORSTER, Philadelphia.

TOPOGRAPHICAL REPRESENTATION OF MUSCLES IN MOTOR CORTEX OF MONKEYS. HSIANG-TUNG CHANG, THEODORE C. RUCH and ARTHUR A. WARD JR., J. Neurophysiol. **10**:39 (Jan.) 1947.

Chang, Ruch and Ward bring an experimental approach to the controversy regarding cortical representation. In order to determine whether muscles or movement patterns are represented in the motor cortex of primates, the authors isolated the muscles about the ankle and obtained kymographic tracings of muscle responses from electrical stimulation of the motor cortex. Not only were individual muscles found to be represented in the motor cortex, but even slips of muscles were observed to have focal points. The flexors were found less responsive than the extensors. A factor in the unresponsiveness of flexor points was inhibition by simultaneous excitation of the extensor points. The authors propose a hypothetic organization of Betz cells into fields with a focus and a fringe, the latter exhibiting overlap.

FORSTER, Philadelphia.

Neuropathology

PRECOCIOUS PUBERTY WITH HYPOTHALAMIC TUMOR (INFUNDIBULOMA). JAMES W. PAPEZ and ARTHUR ECKER, J. Neuropath. & Exper. Neurol. **6**:15 (Jan.) 1947.

Papez and Ecker report the case of precocious puberty in a boy aged 8 who presented physical and sexual development equal to that of 14 years. The ocular signs were dilated pupils and loss of pupillary and accommodation reflexes. Signs of intracranial pressure were headache, dizziness and choked disks. Motor impairment was evident in staggering, incoordination and Babinski and Oppenheim signs on the right side. The patient showed apathy, poor cooperation and marked distractibility. A diagnosis of cerebral tumor was made. The boy was emaciated and chronically ill and did not long survive operation.

Tumors in the posterior part of the hypothalamus are known to produce precocious puberty, especially in young boys. The region of the tuber cinereum, between the mammillary bodies and the stalk of the infundibulum, seems to be the area frequently involved. In this case, Papez and Ecker attempted to determine what parts of the hypothalamic structure were destroyed or spared by a tumor of the third ventricle which had its stalk of origin in the hypothalamic floor just in front of the mammillary bodies.

Necropsy revealed a large tumor (infundibuloma) in the third ventricle attached to the floor in front of the mammillary bodies and to the left thalamus. The pituitary body was grossly normal. Histologic study of the hypothalamic region showed that the median eminence, the ventromedial nuclei and the lateral tuberal nuclei were totally destroyed and the left mammillary body was disconnected and damaged. The left fornix was totally severed near its ending in the mammillary body, and the paraventricular nuclei, the right supraoptic nucleus and a part of the left supraoptic nucleus were spared, but their cells showed unusually severe hyperchromatic reactions without much loss of cells. In the preoptic region the fiber tracts and nucleus basalis were nearly normal, and the lateral preoptic regions and connections to the habenula were intact. The posterior hypothalamic nuclei and descending tracts to the tegmentum were severely injured on the left side, and the optic tracts and supraoptic decussations were badly stretched and damaged. There was a small tumor in the left optic radiation, causing damage in the left geniculate region. The compression of the dorsal thalamus was greatest on the left side, where the internal capsule and the pallidum showed demyelination. Inferences

concerning the neural hypothalamic mechanisms connected with precocious puberty and with other symptoms and conditions are discussed.

GUTTMAN, Wilkes-Barre, Pa.

Psychiatry and Psychopathology

PSYCHOANALYTIC STUDY OF ULCERATIVE COLITIS IN CHILDREN. M. SPERLING, Psychoanalyt. Quart. **15**:302 (July) 1946.

Sperling gives the case reports of 2 children with ulcerative colitis who were treated by psychoanalysis. She found in these cases, and in other cases studied, that there was an extremely ambivalent mother who subjected the child to early and deep frustration, the mother having strong unconscious destructive impulses toward the child. The child reacted with hostile attachment, holding on to the position of a baby with extremely strong oral and anal sadistic tendencies, and was unable to tolerate any psychic tension. The child with ulcerative colitis becomes completely absorbed in its illness, the symptoms being indicative of a narcissistic orientation.

The author found that when these children were hospitalized there was an increase in inflammation, as revealed by proctoscopic examination. She believes that hospitalization represented a traumatic experience to a child and disrupted its narcissistic equilibrium. The mothers reacted with guilt and anxiety as their unconscious wish to get rid of the child was fulfilled.

The children in question are in a state of permanent frustration, which results in a state of unconscious rage with an irresistible urge for immediate discharge. Sperling believes that the specific mechanism in ulcerative colitis is the destruction and elimination of the object through the mucosa of the colon (bleeding). The object having been incorporated sadistically, it is a hostile inner danger and has to be eliminated immediately. The feces and blood come to represent the devaluated and dangerous objects.

The author notes that the severe form of ulcerative colitis shows great resemblance in the patient's behavior, personality structure and dynamics to melancholia. It seems to represent the somatic dramatization of the same conflict.

WERMUTH, Philadelphia.

Diseases of the Brain

SYNCOPE AND SEIZURES. JOHN KERSHMAN, J. Neurol., Neurosurg. & Psychiat. **12**:25 (Feb.) 1949.

Kershman studied 114 patients who had a history of syncopal attacks or similar episodes without loss of consciousness, the spells resembling the vagal or vasovagal attacks described by Gowers. None had definite convulsive seizures, and there was no other evidence of organic disease. The author divided the series into two groups: (1) 92 patients with a history of at least one attack of unconsciousness and (2) 22 patients with no history of unconsciousness. All the patients had abnormal electroencephalograms. In the first group, 65 per cent showed either diffuse dysrhythmia with random slow waves, usually varying from 2 to 6 per second, or mixed fast and slow waves. In this group almost complete absence of alpha waves was characteristic. In 29 per cent there were bilaterally synchronous abnormalities, and in 6 per cent the electroencephalographic abnormality was localized in a discrete cortical area of the temporal region. In the second group, 64 per cent showed diffuse dysrhythmia and 36 per cent bilaterally synchronous

abnormalities of a milder character than in the first group. There were no typical 3 per second wave and spikes in either group. The author is of the opinion that the association of electroencephalographic abnormalities and syncopal spells confirms the fact that in some patients syncope is cerebral in origin and epileptic in character. The absence of alpha waves in 65 per cent of the first group, which were replaced by diffuse slow waves or mixed fast and slow activity, tends to support the hypothesis of Wilson that these attacks originate in the hypothalamic region. The bilaterally synchronous slow waves also indicate a subcortical origin of spells. The term "encephalosyncope" is suggested as a diagnosis for these attacks, which may be regarded as a mild form of idiopathic epilepsy.

N. MALAMUD, San Francisco.

Diseases of the Spinal Cord

ACUTE ANTERIOR POLIOMYELITIS COMPLICATING PREGNANCY. D. M. W. MAXWELL and P. H. WILLCOX, Lanset **2**:353 (Sept. 6) 1947.

Maxwell and Willcox describe the case of a woman in whom acute anterior poliomyelitis occurred during the sixth month of pregnancy. The patient was treated conservatively and allowed to proceed to full term; a normal healthy female child weighing 9 pounds 4 ounces (4,082 Gm.) was delivered. No complications occurred, except that there was delay at the pelvic floor and the child was delivered with forceps. Pregnancy and labor had no adverse effect on the gradual progress of the patient toward recovery of power, nor did the disease affect the expulsive power of the uterine muscle. These observations are in accordance with American experience in similar cases. There is no evidence that the fetus can be infected before delivery. The only cases on record in which fetal death took place before delivery have been due to asphyxiation secondary to respiratory paralysis in the mother. There is evidence that the newborn child has antibodies which protect it from infection in the first few weeks of life. However, a few cases of poliomyelitis in the first month are on record. There is no evidence that interference with pregnancy or cesarean section is indicated in cases of poliomyelitis in pregnant women, except in circumstances which would apply equally to all pregnant women.

J. A. M. A.

Peripheral and Cranial Nerves

DISTURBANCES OF THE ETHMOID BRANCHES OF THE OPHTHALMIC NERVE. J. JEROME LITTELL, Arch. Otolaryng. **43**:481 (May) 1946.

Prompted by dissatisfaction in the care of head pain, Littell made studies of the ethmoid branches of the ophthalmic nerve to determine their importance in rhinologic symptomatology. He emphasizes that mechanical defects of the olfactory fissure produce chronic infections of this area, the pain stimuli being transmitted by the ethmoidal nerves. The symptom complex thus produced he terms the syndrome of the olfactory fissure.

Little emphasis has been placed on irritations of the ethmoidal nerves as the source of pain of rhinologic origin. Most writers stress the importance of the sphenopalatine ganglion and its connections in the conduction of painful stimuli from the intranasal regions. The anatomic relations of the ethmoidal branches make it seem more likely that they, rather than the fibers of the sphenopalatine ganglion, are affected by acute or chronic inflammations closely approximating areas which they traverse. The structure of the narrow, upper part of the nose is such that there is little or no potential space, and pathologic states in that area

are not readily revealed by anterior rhinoscopy. Yet the tissues in this area of the olfactory fissure are five times as sensitive as those within the sinuses themselves.

The characteristic symptom of the syndrome of the olfactory fissure is unilateral or bilateral pain of a dull and continuous character throughout the entire sensory distribution of the ophthalmic nerve. The aching is deep in or about the eyeball, in the frontal region and sometimes at the root of the nose. There is nasal stuffiness, worse on the affected side. Postnasal discharge may be evidenced by an inflamed lateral pharyngeal band, more evident on gagging. There may be systemic symptoms of absorption of toxins. The simple criterion of diagnosis in this symptom complex is the relief of symptoms from shrinking with a mild anesthetic agent.

The author describes 2 cases in which division of the anterior ethmoidal nerve was effective in relieving symptoms. Surgical correction of bad mechanics may be necessary in some cases, but in others removal of predisposing factors and some intranasal treatment may suffice to keep the patient comfortable.

RYAN, Philadelphia.

TINNITUS AURIUM: SOME CONSIDERATIONS CONCERNING ITS ORIGIN AND TREATMENT. MILES ATKINSON, Arch. Otolaryng. **45**:68 (Jan.) 1947.

Pure "tinnitus aurium" refers to the symptom of ringing in the ears. The term is commonly used, however, in referring to all head noises, the causes of which may be extrinsic or intrinsic. Extrinsic tinnitus results from disturbances outside the auditory tract and includes not only extraneous sounds but psychogenic disturbances. Intrinsic, or true, tinnitus is the result of a disturbance within the auditory tract itself and is always evidenced by impaired hearing at the time the tinnitus is present. Atkinson considers tinnitus as an auditory paresthesia resulting from a lesion of the infrasegmental portion of the auditory tract, probably of the nerve trunk. This theory could explain many of the perplexing features of cryptogenic tinnitus.

Clinical experiments were performed which indicated the vascular nature of the disturbance. Patients with vasospastic mechanism who showed normal cutaneous reactions to histamine were treated with nicotinic acid, with resulting vasodilatation and temporary improvement in a significant percentage of cases. Vasconstrictors, on the other hand, produced aggravation of the tinnitus. The histamine-sensitive patients reacted well to histamine desensitization but disastrously to vasodilators. On the basis of this theory of a vascular origin of tinnitus, the method of treatment by inflation of the eustachian tube is regarded as irrational unless definite occlusion is evident.

The cause of tinnitus may be difficult to determine, as when allergens are responsible. When discovered, the cause may not easily be removed. Irretrievable damage may already have been done, as in cases of vasospasm, in which the vessel walls may have been so damaged that response to vasodilators is poor. If the vasospastic theory is accepted, it is important that prompt and adequate treatment be instituted to forestall the onset of deafness.

RYAN, Philadelphia.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY, SECTION OF NEUROLOGY AND PSYCHIATRY OF THE DISTRICT OF COLUMBIA MEDICAL SOCIETY AND THE NEUROPSYCHIATRIC SECTION OF THE BALTIMORE COUNTY MEDICAL SOCIETY

Anthony S. Tornay, M.D., *Presiding*

Joint Meeting, Oct. 24, 1947

Aneurysms of the Posterior Communicating Artery: Report of Five Cases with Operation. DR. RUDOLPH JAEGER.

Five cases in which operation revealed aneurysm of the posterior communicating artery of the circle of Willis were reported. In 4 of the cases cure was effected by clipping the arteries running into the aneurysms. The largest aneurysm was approximately 2.5 cm. and the smallest 1 cm., in diameter.

In 4 cases there were the classic symptoms of spontaneous subarachnoid hemorrhage with sudden generalized headache, later localizing to the eye and supraorbital region, with stiffness and pain in the legs and neck, and nausea. In each of the 4 cases, at the onset of headache or soon after, paralysis of the third cranial nerve developed. In 1 case there was no headache, but paralysis of the third nerve was present. In all cases evidence of hemorrhage from rupture of the aneurysm was disclosed by discoloration of the cerebral cortex or by blood in the spinal fluid.

In 2 cases the aneurysm was disclosed by arteriography; in 2 cases the contrast medium failed to show the lesion, and in 1 case no angiogram was made.

Since the ultimate mortality from untreated intracranial aneurysm must be close to 100 per cent, it is necessary to attempt surgical cure of this lesion. Sudden headache, generalized or localized to the eye or the supraorbital region, accompanied with a paralysis of the third nerve, localizes the lesion to the intracranial position of the third nerve, back of the carotid artery. In this location, an aneurysm of the carotid or the posterior communicating artery must be suspected, and such symptoms are sufficiently localizing and diagnostic to warrant surgical exploration.

The procedure of arteriography is not accurate enough to be dependable as a positive diagnostic test. Clinical examination alone should determine the diagnosis.

As shown by these 5 cases, craniotomy, exploration and ligation of the supplying arteries are both feasible and life saving, since there was only 1 death in the 5 cases.

DISCUSSION

DR. WALTER FREEMAN, Washington, D. C.: Dr. Jaeger sent me a copy of this paper, and I was delighted beyond measure to know that something could be done in these cases. Neurologists have been rather helpless before the neurosurgeons showed a way of handling them. Of course, we are familiar with Dandy's pioneer exploits in the treatment of aneurysms, but in the case of the little thin-walled aneurysms, I have heretofore felt pretty hopeless.

I wonder whether the cerebral circulation will stand either a clip or a temporary ligature on the carotid artery during the operation to prevent flooding of the wound at the time of operation? I believe that Dr. Jaeger mentioned the desir-

ability of compression of the carotid artery so as to establish a tolerance of the brain tissue to the anemia.

A few years ago I sounded off too soon. I reported a case of symmetric cerebral aneurysm with rupture and recovery. A young Irish girl sustained her first rupture in 1931, the aneurysm paralyzing the right third nerve. She had the usual symptoms of subarachnoid hemorrhage. She recovered. The ptosis improved, so that she was able to raise the eyelid voluntarily, although there was considerable drooping and she experienced an annoying diplopia, for which she wore a frosted lens. The second attack occurred in 1939 and paralyzed the other oculomotor nerve. By this time the first side was functioning adequately. The third attack occurred in March 1942, and she died. There was no autopsy.

I think that if I had known then what I know now about these aneurysms, I should have had an arteriogram and have attempted to overcome this dreadful disorder.

Before Dr. Jaeger completes this series of cases he is going to study in the future, he is going to run into the symmetric aneurysm, and that will cause him trouble.

Dr. Francis J. Otenasek, Baltimore: Those of us who are personally familiar with the tremendous technical problems involved in the surgical therapy of intracranial aneurysms will know at once what a really great achievement Dr. Jaeger has made, for this work represents a milestone in advancement in the surgical field.

I should like to emphasize that his cases represent the very first aneurysms of the posterior communicating artery which have been treated successfully, and it is almost unbelievable that he has actually cured 4 of 5 patients with this condition.

There are two factors of great significance in this work. The first, as he points out, is that pain in the eye may result from pressure of an aneurysm against the tentorium cerebelli. This observation is one of great significance, because it was heretofore believed that pain in the eye resulting from an aneurysm came almost invariably from one situated far forward on the carotid artery, which actually was exerting a pressure effect on the fifth nerve, chiefly on the first branch. It has been shown that on stimulation of the tentorium pain is referred to the orbit.

As Dr. Jaeger also said, arteriography does not always localize these aneurysms on the posterior communicating artery and that if one realizes the significance of the pain in the eye their localization becomes a great deal easier.

The second factor of great significance is Dr. Jaeger's perfection of an operative approach permitting adequate visualization of this area, which is extremely difficult to get to. He does this by the use of a large bone flap, as he said, and, in addition, something which I do not think he mentioned today, use of a lumbar puncture needle to help drain out spinal fluid during the course of the operation and so create more room intracranially. In this way he gets a good exposure of both the anterior and the middle fossa.

In previous attempts, when one exposed the circle of Willis, it was limited to the anterior fossa and the most anterior portion of the middle fossa, so that one could see the internal carotid, the middle cerebral and the anterior cerebral artery and only a tiny portion of the posterior communicating artery.

I am sure that this exposure, which enables one to see both the anterior and the middle fossa, results in finding the aneurysms which had previously been missed or which had previously been falsely localized to the internal carotid artery.

Since the publication of Dr. Dandy's monograph (Intracranial Arterial Aneurysms, Ithaca, N. Y., Comstock Publishing Co., Inc., 1944), my colleagues and I have had 2 cases of supposed aneurysms of the posterior communicating artery. In 1 of these cases hemorrhage occurred into the temporal lobe; we made the

usual anterior approach and failed to find any aneurysm in the anterior portion of the circle of Willis. By enlarging the approach and going through the temporal lobe, we were able to remove an aneurysm presumably of the posterior communicating artery.

In the second case ligation of the carotid artery was carried out intracranially and in the neck. The aneurysm was visualized and was thought to arise from the internal carotid artery. We therefore thought that the aneurysm was trapped by the dual ligature. However, two months after operation the patient had another subarachnoid hemorrhage, with no evidence of slipping of the silver clip; and we now believe that the aneurysm was probably on the posterior communicating artery, and not on the carotid artery at all.

The work which Dr. Jaeger here reports requires not only a superb operative skill, but tremendous courage.

I should like to ask him one or two questions. Does he have any age limit within which he operates on patients for intracranial aneurysm, and are there patients who tolerate compression of the carotid artery well regardless of age? Second, does he ever advocate bilateral exploration of the circle of Willis in cases of repeated subarachnoid hemorrhage in which the aneurysm has not been localized by arteriography?

Dr. Henry T. Wycis: Dr. Jaeger is to be commended on his surgical skill in attacking these serious problems. Does he feel that these anomalies might be easily approached by resection of the temporal lobe, particularly on the right side?

Three years ago, before the Philadelphia Neurological Society, I reported a case of aneurysm of the posterior communicating artery. During an episode of progressive bleeding, hemorrhage was controlled by placing a clip on the internal carotid artery within the skull.

Dr. Robert H. Groh, Washington, D. C.: The reports from various investigations in the field of arteriography confirm Dr. Jaeger's experience that the posterior communicating artery is not often seen with an injection of the internal carotid artery. However, the percentage of pictures of the posterior communicating artery is higher if the posterior fossa is visualized by injection into the vertebral artery.

We have done several of these injections in Washington for aneurysms in the posterior fossa and have demonstrated 2 of them. The technic is really an exposure of the subclavian artery, and on distal compression of the subclavian artery the opaque medium passes into the vertebral artery.

I am wondering, therefore, whether such an approach might not more adequately disclose the lesions which Dr. Jaeger described.

Dr. O. C. Solnitzky, Washington, D. C.: I should like to ask Dr. Jaeger whether he has any opinion about the cause of these aneurysms. Two theories of the origin of congenital cerebral aneurysms exist: (1) They are due to a prenatal defect, and (2) they are due to remnants of embryonic vessels (Dr. Dandy's theory).

I have made serial sections of all branches of the circle of Willis, both in length and in bifurcation, and have found no evidence of either prenatal defects or of embryonic remnants.

In some cases of aneurysm of the posterior communicating artery there has been pressure on the optic tract with homonymous hemianopsia. Did Dr. Jaeger find any evidence of this in his cases?

DR. RUDOLPH JAEGER: I think that temporary occlusion of the carotid artery during operation will be a valuable addition to the surgical approach to these lesions. There are many technical maneuvers that need perfecting.

If there is an intracranial hemorrhage which is thought to be from an aneurysm, and there are no localizing symptoms, what is the proper diagnostic approach to the problem? In the light of present knowledge of the great mortality from these lesions, I believe that their localization with arteriography should be attempted, even though bilateral injection of the internal carotid artery, and perhaps of one subclavian artery, may be required to visualize completely the cerebral circulation. That can be done, as has been described. Perhaps the point has been reached where such injections should be made to complete the diagnostic information in every case of spontaneous subarachnoid hemorrhage

Resection of the temporal lobe, particularly on the right side, may possibly provide more ready access to this relatively inaccessible region.

In older persons arteriosclerosis is the common cause of aneurysm. In these patients it is wise to proceed cautiously with any treatment of carotid occlusion. In younger persons aneurysms are usually congenital. The collateral circulation is likely to be adequate, and ligation is reasonably safe if the patient tolerates temporary occlusion tests. From a fifteen minute pressure test one cannot be certain that the cerebral circulation is adequate in an elderly person. In many such patients two, three or four days may elapse after ligation of the carotid artery before a hemiparesis develops.

Physiologic Studies on Arteriovenous Anomalies of the Brain. DR. HENRY A. SHENKIN, DR. EUGENE B. SPITZ (by invitation), DR. FRANCIS C. GRANT and DR. SEYMOUR S. KETY (by invitation).

Determination of the cerebral blood flow by the nitrous oxide technic of Kety and Schmidt revealed notable increases in 2 instances of large arteriovenous anomalies of the brain. In 1 case the cerebral blood flow was found to be 143 cc. per hundred grams of brain per minute, and in the other it was 185 cc. The average normal flow had previously been established as 54 cc. per hundred grams of brain per minute in a large series of healthy young men. The cerebral metabolic activity, determined in terms of oxygen consumption, was well within the normal range in each patient. The cardiac outputs in the 2 patients, recorded on the ballistocardiograph, were, respectively, 39 and 30 per cent higher than the average normal for persons of similar heights and weights. The mean arterial blood pressure, measured directly with a damped mercury manometer, was consistently lower than normal, being 79 mm. of mercury for the first patient and 71 mm. of mercury for the second. This decrease was particularly reflected in lower diastolic pressures (56 and 65 mm. of mercury), as obtained on repeated occasions by the auscultatory method. An enlarged heart was noted in each patient on fluoroscopic examination. The plasma volume, as estimated by the dye dilution method of Gibson and Evelyn, was normal for 1 patient and increased 13 per cent for the second. The interrelation of these observations and their utilization in the diagnosis of arteriovenous anomalies of the brain were discussed.

DISCUSSION

DR. O. C. SOLNITZKY, Washington, D. C.: Arteriovenous anastomoses are of very different types. They may be classified as normal and pathologic. Normal arteriovenous anastomoses are found in fingers and in other parts of the extremities of man. They have been demonstrated in the tongue of the dog and in the ear

of the rabbit. They are characterized by the presence of three parts: a proximal, or arterial, portion; a distal, or venous part, and an intermediate portion. The action of these normal arteriovenous anastomoses seems to be that of control of local circulation.

Pathologic arteriovenous connections may be small or large. I have seen small ones on the face and in the abdominal and thoracic cavities. The large arteriovenous anastomoses in the brain, as is generally known, are not very common. The cause of these arteriovenous connections in the brain is of interest. Several facts should be kept in mind.

First, in the majority of cases these large arteriovenous connections occur in the field of the middle cerebral artery. They have been found in the field of the anterior cerebral and the posterior cerebral artery, but they are by far the commonest in the field of the middle cerebral artery.

Second, they are always surface lesions. In an attempt to reach a possible explanation of this fact, the gross anatomy of the middle cerebral artery may be considered. The stem of the middle cerebral artery, while it lies in the depth of the cistern of the sylvian fissure, shows many variations in its branchings. There may be only two or three branches, or there may be as many as twelve. Accompanying the middle cerebral artery is the middle cerebral vein. The middle cerebral vein also shows many variations. Of course, its chief function is to provide venous drainage as far as the motor area of the face. There a connection exists between the tributaries of the middle cerebral and the superior cerebral vein. It is possible that in some cases, with the large number of branches of the middle cerebral and the large number of tributaries of the middle cerebral lying in close proximity in the cistern of the sylvian fissure, they might in some way become connected.

Embryologically, the cerebral circulation begins as a system of disconnected blood islands, which gradually become lumenized through liquefaction, and the first blood vessels on the surface of the brain are of a capillary plexus type. It is only subsequently that this capillary plexus differentiates into arteries, capillaries and veins. While it is impossible to tell exactly how these connections arise, it is probable that in those early days an obstruction to the venous return of the tributaries of the middle cerebral vein may develop.

Since no symptoms arise from these arteriovenous connections in the brain until about the second or third decade of life, and since in the rest of the body arteriovenous connections of a large size are always of traumatic origin, it may be possible that as a result of trauma, or merely by pressure alone, the branches of the middle cerebral and the tributaries of the middle cerebral vein may become connected and in that way produce arteriovenous connections.

I should like to congratulate the authors, because to my knowledge this is the first attempt to apply sound physiologic principles to the diagnosis of clinical signs so far as arteriovenous anastomoses is concerned. Practically all such anastomoses produce cerebral symptoms, and if it is kept in mind that an increased cerebral blood flow, increased cardiac output and a lower blood pressure accompany these large anastomoses the existence of this anomaly will be kept in mind.

DR. HENRY WYCIS: I should like to ask Dr. Shenkin whether he and his co-workers have any data on the solubility coefficient of the nitrous oxide? This, apparently, is a variable and differs with the individual subject. Might not such a variable factor alter the end result of the cerebral blood flow in these cases?

DR. HENRY A. SHENKIN: I can answer that by saying that Dr. Kety has investigated this question thoroughly and that it is the subject of a paper to be

published shortly. He found the brain-blood partition coefficient to be unity in studies on dog and man in vitro and in vivo and in a variety of pathologic conditions.

Vascular Abnormalities and Tumors of the Spinal Cord. Dr. J. C. Yaskin, Dr. C. I. Oller, Dr. R. A. Groff and Dr. H. A. Shenkin.

The 6 cases reported on comprised 3 cases of vascular abnormalities in the nature of masses of dilated vessels, chiefly veins, and 3 cases of actual tumors of vascular origin. Of the tumors, 2 were hemangioblastomas and the third was a hemangioendothelioma. The venous abnormalities were localized as follows: 1 at the eleventh and twelfth thoracic; 1 at the twelfth thoracic and first lumbar and 1 at the fifth to the seventh cervical segment. The tumors were distributed as follows: 1 was at the fifth lumbar; 1 at the third thoracic and 1 at the second cervical to the first thoracic segment.

All 3 of the varices were subdural, although 1 was evident in both the epidural and the subdural space. Of the neoplasms, 1 was epidural, 1 intradural and 1 intramedullary. .

The commonest and most prominent symptom of this entire group was severe pain of the radiating type. Other symptoms were inconstant and, when present, consisted of muscular and sensory disorders of the extremities. All symptoms were characteristically remittent. There were no associated nevi of the skin or other structures.

Myelographic studies revealed a filling defect in each case, but only in 2 was the abnormality sufficiently characteristic to suggest the vascular nature of the lesion.

From our own experience, the clinical findings were of little help in an etiologic diagnosis. However, in retrospect, severe, remittent, radiating pain in the presence of vague clinical or roentgenologic findings should create the suspicion of a vascular lesion of the spinal cord.

The venous anomalies were not materially altered by operative intervention, which consisted of decompression and/or electrocoagulation of the vessels. Postoperative roentgen therapy was likewise of no benefit.

Of the cases of vascular tumors, partial surgical removal resulted in definite improvement in 1 case and rendered the tumor stationary in another, so that seven years after operation the patient's status has not materially changed. The third patient, who had a hemangioendothelioma, died of widespread metastases.

DISCUSSION

Dr. James G. Arnold Jr., Baltimore: The authors have presented an interesting and instructive series of cases. Vascular tumors of the spinal axis are frequently difficult to diagnose, either clinically or with contrast mediums. Such tumors constitute only a small percentage of tumors of the spinal cord, the proportion ranging from 3 to 5 per cent in different series, but we can all recall cases of pain in the back in which we were unable to make an etiologic diagnosis. Dr. Yaskin has stressed the point that with persistent pain in the back, in the absence of other evidence, a vascular tumor should be considered. Dr. Yaskin further mentioned the advisability of repeated myelograms in cases of pain in the back of obscure origin.

I should like to emphasize a statement which was made by Elsberg in 1925, that is, when the presence of vascular anomaly is suspected at operation, one should not accept the diagnosis immediately, for there may be a tumor beyond the exposed field which is responsible for the vascular changes. I recently had such

an experience, and by running the catheter higher I came on an obstruction which proved to be a neurofibroma. As is evident from the statistics presented today, the treatment is unsatisfactory. The reason is immediately apparent in the photographs of the tumors which were presented. Direct surgical attack on these lesions is apt to be disastrous. I recently exposed an extensive plexiform angioma in the cervical region in a patient with quadriplegia. The dura was left open for decompression. Improvement in function began shortly after operation, before roentgen therapy was given. In the treatment of vascular lesions of the spinal cord roentgen irradiation has been widely used. The results in Dr. Yaskin's cases indicate that roentgen ray therapy is of questionable value.

DR. O. H. FULCHER, Washington, D. C.: When one comes to a medical meeting in this city, the oldest medical center in the United States, one is always inspired and enlightened by the scientific papers. This trip and this paper represent no exception.

On the way here, Dr. Solnitzky reviewed the anatomy of the epidural venous plexus, which receives the venous blood from the cord and which is connected with the regional veins. There are no valves present. Consequently, the intravenous pressure of these epidural veins is largely dependent on intra-abdominal pressure. Hence, there exist good anatomic and physiologic bases for the development of varicosities. It is possible that some of the painful conditions of the back could be due to these varicosities, which are difficult to diagnose. Dr. Solnitzky has suggested that the dorsal vein of the penis be used to obtain epidural phlebograms.

Dr. P. J. Gallagher stated that a few years ago he explored the epidural spaces and found a large varicose vein in the upper dorsal region compressing a nerve root. The preoperative diagnosis had been a ruptured intervertebral disk. On reviewing the clinical data, he learned that the patient had suffered from pain only on lying down and that spinal puncture had revealed a block to the flow of spinal fluid only when lying down. He reasoned that the varicosities were engorged only when the patient was recumbent.

During the past year I have operated in 3 cases of epidural or intrathecal varicosities. A correct diagnosis was not made before operation in any instance. Exploration in 1 case revealed varicosities involving the conus, which were not disturbed. Later, the patient was advised to wear no tight-fitting clothes or girdle and to get into the knee-chest position several times daily. In another case, of varicosities of the epidural veins, because of profuse hemorrhage some of the veins were cauterized, with the result that the condition was made worse. In the third case, of intrathecal varicosities of the lower cervical region, although the varicosities were not disturbed and the dural arachnoid membrane was left open, the neurologic status was made worse by operation.

Let us hope that Dr. Yaskin's excellent article will stimulate us to renewed vigor in endeavoring to diagnose vascular anomalies of the spinal cord, so that surgical exploration may not be required.

DR. FRANCIS C. GRANT: My only comment on these cases concerns what not to do. I think that any interference with the veins about the cord is a dangerous procedure. In the case represented by Dr. Yaskin's first slide, that of the hemangioma or venous angioma of the cord, I attempted to coagulate the vessels. That was necessary because when the dura was opened one of the veins ruptured. Electrocoagulation changed a partial into a complete lesion of the spinal cord, from which the boy did not recover.

I think, therefore, that in these cases it is essential that one temper one's justice with mercy and do as little as possible. My own feeling is that with venous

anomalies or any vascular anomaly of the cord, the most that should be attempted is decompression, by opening the dura, no attempt whatever being made to extirpate, or in any way to interfere with, the vessels involved.

A striking feature of these cases is the remission and recurrence of symptoms. I remember well a prominent physician in this city who complained of pain in his legs. He was a great fisherman, and every time he went fiishing he would have pains in his legs and have to come home. He was looked on as neurotic, in spite of the fact he liked to fish and was doing what he liked when these pains bothered him.

I was finally asked to see him in consultation, and Dr. Foster Kennedy came over from New York in consultation. Dr. Kennedy looked at the patient and made a flat diagnosis, without any peradventure of a doubt, that the man had a hemangioma of the cord and advised roentgen irradiation. Unfortunately, the patient was operated on and died. Autopsy revealed a hemangioma of his cord. That was as pretty a clinical diagnosis as I had ever seen.

I believe that these patients have remissions; they go along for a while and they begin to have pain; then they rest and the pain disappears. It may well be, as was proposed, that abdominal pressure with dilatation of the veins on exertion and the subsequent relaxation and draining of the veins on rest may have a great deal to do with this variation in symptoms. These patients who have vague pains in the back which come and go, and are likely to be severer on exertion and are relieved by rest, and who eventually show a myelographic defect, are subjects for operation because one cannot be certain of what is there until one has looked. But if a venous anomaly is found, my strong advice is to leave it alone and to be satisfied with a decompression. Roentgen treatment may be of benefit. I do not know. It has not been strikingly so in the cases I have seen; certainly, it is much better to rely on roentgen irradiation than it is to attempt by surgical means to extirpate the lesion, with the very good chance of changing a partial lesion of the cord into a complete lesion.

Dr. Robert A. Groff: I have nothing to add to what Dr. Grant has already said; I wish simply to emphasize that one should not treat anomalous venous lesions of the spinal cord surgically.

In the 1 case reported by Dr. Yaskin, there was a hemangioblastoma at the level of the fifth lumbar segment. From this lesion, extending upward to the level of the first lumbar vertebra, was a mass of dilated veins which filled the entire dural sac. When the tumor was removed, it was necessary to remove the dilated veins. There is no doubt in my mind that by the removal of these veins the blood supply to the roots was so impaired that it caused the saddle anesthesia and loss of vesical and rectal function. The exposure of this lesion was attended with horror, for a myelographic examination had been performed, the needle entering the subarachnoid space between the third and the fourth lumbar vertebra. When the dura was opened at this level, the large dilated veins were seen directly beneath it, so that practically no space existed between the dura and the veins. I shudder to think what would have happened had the pantopaque® been injected into the veins themselves.

If the diagnosis of a venous anomaly can be made by roentgenogram or contrast myelograms, one should use roentgen ray therapy rather than surgery.

Pick's Disease: General Survey and Report of a Case with Chronic Chorea. Dr. N. W. Winkelman.

Circumscribed cerebral atrophy, lobar atrophy or Pick's disease is usually considered an heredodegenerative disease (Malamud and Waggoner), and it is probably dependent on an "involutional" process. The atrophic areas do not correspond to vascular distributions.

Vascular disease, if present, is not a necessary component of the pathologic symptom complex. The symptoms may be divided into three general groups: (1) symptoms occurring as the result of involvement of the frontal lobe, (2) symptoms due to atrophy of the temporal lobe and (3) symptoms resulting from shrinkage of the subcortical ganglia.

This presentation is concerned with the last group of symptoms. The importance of symptoms referable to the extrapyramidal system in Pick's disease was revealed by the observation at autopsy of atrophy of the striopallidonigral system in a case of Pick's disease.

Only 3 previous presentations on this subject have been made, beginning with the paper by Braunmühl in 1930 (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **124**:214, 1930).

The case presented in moving pictures was that of a white woman aged 42, whose disease began approximately eleven years before my first examination, with a progressive organic dementia. Later, signs of involvement of the temporal lobe made themselves manifest as the patient lost her ability to read, write and comprehend. The family history gave evidence of psychiatric problems in the family. The patient's aunt is at present in the Norristown State Hospital, with a condition diagnosed (according to Dr. Arthur P. Noyes) as "cerebral arteriosclerosis."

Examination of the patient on May 20, 1947 showed a true organic psychosis. She had difficulty in making herself understood because of jargon aphasia. She was unable to write. Her attire showed neglect and indifference. She walked on her heels with her hands held together, and there were coarse, irregular choreic movements of the upper half of the body; when she was sitting the movements were also noticeable in the lower limbs. The cranial nerves, so far as they could be tested, were normal. There was a general hyperreflexia, without pathologic signs. Sensation could not be tested for. The blood pressure was 140 systolic and 70 diastolic.

A pneumoencephalogram, done in June 1947, showed internal hydrocephalus and severe cortical atrophy of the frontal and temporal lobes bilaterally. A complete laboratory study revealed nothing significant. An electroencephalogram gave indication of strikingly abnormal waves over both frontal lobes, particularly on the right. In addition, the temporal, parietal and occipital lobes were involved, to a lesser degree.

The diagnosis was Pick's disease, with atrophy of the frontal and temporal lobes, and choreic movements, the result of shrinkage of the subcortical ganglia. It was thus felt that the patient had symptoms of involvement of the subcortical ganglia associated with cortical manifestations.

This case confirms our suspicions, based on previous histologic studies in 2 cases in particular, that the subcortical ganglia can be involved in the same type of atrophic change as is observed in the frontal and temporal lobes. The whole condition is considered an involutional process. It may be limited to the cortex, as it usually is, but may also attack the subcortical ganglia. Its relation to Huntington's chorea was discussed in view of the fact that both may be hereditary, both degenerative and both attack the same parts of the central nervous system.

DISCUSSION

DR. SAMUEL HICKS: I have been asked to discuss Pick's disease of the brain from the point of view of the pathologist. Those who have studied the disorder closely believe that it represents a clinicopathologic entity, although there is some discrepancy in the criteria for judging the presence of the disease at autopsy. The criteria often cited are: (1) localized cerebral atrophy, oftenest of the frontal, temporal and insular regions, often symmetric; (2) microscopic changes in the

cortical neurons, characterized by a peculiar cytoplasmic swelling and by cytoplasmic inclusions, which stain with silver. None of these changes is absolutely pathognomonic.

In addition, there are some general atrophy and diffuse gliosis. Anatomic vascular disease and Alzheimer's neurofibrillary change are said to be absent. Since the patients are usually between 40 and 60 years of age, arteriosclerotic disease of the brain must always be carefully ruled out. It is now well recognized that the cause of diffuse, as well as severe focal, arteriosclerotic disease of the brain may be superimposed circulatory failure of cardiovascular origin. This pattern, too, must be ruled out by the pathologist in differentiating Pick's disease, for it occurs sometimes when arteriosclerosis of the brain is not severe.

That the pathogenesis of Pick's disease is unknown is evidenced by the many theories proposed to explain it. A "heredodegenerative" nature is suggested by the frequent symmetric involvement of areas of the brain which are phylogenetically recent. A congenital or acquired metabolic defect is assumed for these systems. Sometimes the disease has familial distribution.

The patchy and well demarcated regions of myelin and nerve cell destruction in some cases led Ferraro to suggest vascular spasm as a cause.

To me, there are two interesting features of Pick's disease, both nonspecific: The first is the diffuse gliosis—a proliferation of fibrillary astrocytes, which is evidence of reaction to some type of injury. The second is the destruction of cortical neurons, especially the outer layers, which are among the most vulnerable of all nerve cells. Such changes are seen in the reaction to injury following chronic anoxia, hypoglycemia and systemic toxic or metabolic injuries. It will, therefore, be interesting to see whether Pick's disease is found to be a manifestation of a definite systemic metabolic disease, either hereditary or acquired. Experimental work now being conducted in our, and other, laboratories on the elective susceptibility of certain parts of the nervous system to different kinds of injury may throw light on Pick's disease.

DR. N. W. WINKELMAN: I did not attempt to discuss the histopathology of Pick's disease in this paper. I am grateful, however, that the pathology was touched on. I do not believe, however, that the presence of arteriosclerosis or its absence means anything in the diagnosis of Pick's disease. I do not believe that anyone has ever seen arteriosclerosis as the etiologic factor in an atrophy so delimited bilaterally as that seen in Pick's disease. In a paper read before the American Association of Neuropathologists (*J. Neuropath. & Exper. Neurol.* **8**:30, 1949) Dr. Book and I reported the case of a young woman physician, who died at the age of 34 and who showed as advanced arteriosclerosis as one sees in the ordinary patient of 80. We did not believe, and I still no not believe, that the arteriosclerosis played a part in the production of Pick's disease. It may have been part and parcel of what Wilson called an "involutional process" or what Gowers called an abiotrophy.

One has still much to learn about the etiology of Pick's disease, but it is certainly true that an increasing number of cases are being described in families. Kerback reported the disease in 2 sisters, but they had Huntington's chorea in addition; so there may be a combination of conditions that are heredodegenerative.

Role of the Neurologist in the Medical Program of the Veterans Administration. DR. PAUL R. HAWLEY, Washington, D. C.

The primary role of the neurologist in the medical program of the Veterans Administration is to administer expert professional care to neurologically disabled

veterans. Statistics, though incomplete, have permitted sound estimates of the need. At least one third of neuropsychiatric patients in general hospitals have primarily neurologic disabilities, and from 15 to 30 per cent of neuropsychiatric patients in special neuropsychiatric hospitals suffer from some sort of organic nervous disorder. Twenty thousand veterans have neurologic residual of injuries to the brain, and about 3,000, of injuries to the spinal cord. Approximately 50,000 epileptic veterans will require study and treatment during the next ten years, and at least 12,000 veterans will have symptomatic neurosyphilis over a spread of 25 years. This estimate of the present census will undoubtedly expand, with factors of time and age. The interesting patient material, the opportunity to participate in the largest program for medical follow-up studies in history and the good remuneration for neurologists as consultants, attendants or full time physicians, as well as the opportunity to give service in a worthy cause, are some of the advantages presented.

The task of the Administration is to recruit a pool of the best possible neurologic and psychiatric talent for the care of neuropsychiatric veterans. In order to provide these patients with the best neuropsychiatric care, we have organized centrally a neuropsychiatric division under an over-all neuropsychiatric chief; this division is subdivided into sections in psychiatry, neurology and clinical psychology, which have been integrated so far as possible into a single organic unit. In addition to the supervision and care of neurologic patients, the neurologist in the Veterans Administration also has the task of rounding out the general neuropsychiatric program by examining and recommending treatment, by supplying the connecting link between psychiatry and internal medicine and by keeping psychiatry in contact with the basic sciences of neuropathology and neurophysiology.

The care of many of the special groups of patients—the paraplegic and the aphasic patients, and those with post-traumatic epilepsy—requires intensive study both from the medical and from the surgical standpoint. In order that the best results may be obtained from the combined skills of both neurologists and neurosurgeons, neurologic services have been established in close proximity to neurosurgical services, so far as possible. To the neurologist are assigned the preliminary diagnostic procedures and the postoperative convalescent care, and to the neurosurgeon, the operative procedures. To integrate this service further, neurologist and neurosurgeon are encouraged to make ward rounds together, and residents in neurology rotate for short periods through the neurosurgical service, and vice versa.

The Veterans Administration has instituted a pilot program under the department of neurology of the University of Minnesota for the rehabilitation of patients with chronic neurologic disorders at the Veterans Hospital in Minneapolis, designed to restore them to a useful life. During the first six months of this program, 70 per cent of a group of 80 patients, some bedridden for ten years, were rendered capable of self care; and, of these, 35 per cent were discharged. The condition of only 5 per cent was considered hopeless. This was a victory for competent medical care, and also a forward step economically, since it made available urgently needed beds. The favorable results of this initial step augur well for expanded efforts in this field. The neurologist of the Veterans Administration is the logical supervisor of such a program.

National programs have been devised for the study, treatment and training of patients with epilepsy and aphasia for the specific purpose of helping them to lives of greater usefulness to themselves and to society. Neurologists of the Veterans

Administration have been placed in charge of these programs, and the scope of treatment includes not only the pathologic factor, but the psychologic and sociologic factors as well.

Qualified neurologists are urgently needed in the resident training program. Under the Veterans Administration, eight resident training programs have been set up for neurologists or neuropsychiatrists predominantly interested in neurology. They are in Veterans Administration hospitals under the auspices of the leading neurologic services of approved medical schools in accordance with our Deans Committee plan, and they also include supplementary professional courses in specialized neurologic activities. Residents trained in the Veterans Administration are expected to remain in the Administration as full time physicians at least for the interval between completion of training and certification by specialty boards. We hope that our services will reach such a level of proficiency that it will be an inducement to many to stay permanently in the Veterans Administration as chiefs of neurologic services in hospitals.

News and Comment

GRANT FOR TRAINING IN PSYCHIATRY, WALTER E. FERNALD STATE SCHOOL

The United States Public Health Service under the National Mental Health Act has approved a grant for a trainee in psychiatry at the Walter E. Fernald State School, situated 8 miles from Boston. The stipend is for level 5, or $3,000 per year. However, candidates at lower levels may be considered and the amount of the stipend adjusted to the level of the candidate's training. Training will be offered in mental deficiency, child psychiatry and related psychiatric and neurologic problems through supervised experience in the outpatient and inpatient departments, the research laboratory, and the psychologic, educational and social service departments, as well as participation in staff meetings, seminars in basic psychiatry and neurology and in child psychiatry.

Applications, including the applicant's qualifications, or requests for further information, should be forwarded to Dr. Malcolm J. Farrell, superintendent, Walter E. Fernald State School, Waverley 78, Mass.

REVISED EDITION OF "REVIEWS OF MEDICAL MOTION PICTURES" NOW AVAILABLE

The Committee on Medical Motion Pictures has completed the first revised edition of the booklet entitled "Reviews of Medical Motion Pictures." It now contains all the film reviews published in *The Journal of the American Medical Association* up to Jan. 1 1949. It also includes a classified table of contents, as well as a list of motion pictures available through the Motion Picture Library, American Medical Association.

The purpose of the reviews is to provide a brief description and evaluation of motion pictures which are available to members of the medical profession. Each film is reviewed and commented on by competent authorities.

Copies are available on request from the Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10.

PUBLICATION OF *ARCHIVOS DE HISTOLOGIA NORMAL Y PATOLOGICA*

After a lapse of a few issues, the *Archivos de histología normal y patológica* will again appear regularly. It is planned to have an article by Río del Hortega in each of the coming issues. Subscriptions may be obtained by writing to Dr. M. Polak, director, Fundación Roux, 81 Montevideo, 3rd Piso, Buenos Aires, Argentina.

NEW DIRECTOR OF RESEARCH PROJECTS, NATIONAL INSTITUTE OF MENTAL HEALTH

The resignation of Dr. Lawrence Kolb as director of Research Projects for the National Institute of Mental Health, and the appointment of Dr. John Eberhart to that position, effective July 1, was announced today by Surgeon General Leonard A. Scheele, Public Health Service, Federal Security Agency.

Dr. Kolb has accepted a position as consultant in psychiatry at the Mayo Clinic, Rochester, Minn.

Dr. Eberhart has been chief psychologist of the Training and Standards Branch of the National Institute of Mental Health. Prior to joining the Public Health

Service staff in 1947, he was chief of the Research Design Section, Surveys Division, Veterans Administration. He was formerly a member of the psychology faculty of Northwestern University and, for two years, was a postdoctoral fellow of the Social Science Research Council. He served as a naval officer during the war.

As director of Research Projects, Dr. Eberhart will administer the program of grants in aid for research in the mental health field.

NEUROSURGICAL SOCIETY OF AMERICA

On June 5, 1948, in Chicago, the Neurosurgical Society of America was founded, and on July 8 the society was incorporated in the State of Illinois. Its first annual scientific session was held in Chicago, Nov. 19 and 20, 1948. This year's meeting will be held on October 30, 31 and November 1, at the Chateau Frontenac in Quebec City, Quebec, Canada.

The following officers were elected at the first scientific session: Dr. Arthur A. Morris, Washington, D. C., president; Dr. Frank Otenasek, Baltimore, vice president; Dr. Edward Schlesinger, New York, secretary, and Dr. I. J. Speigel, Chicago, treasurer. Counselors are Dr. Douglas Hawks, Memphis, Tenn.; Dr. George Roulhac, St. Louis; Dr. Edward Schlesinger, New York; Dr. Joseph Dorsey, Boston, and Dr. Jack Woolf, Dallas, Texas.

Application forms for membership in this society may be had by writing the secretary. Membership is open to neurosurgeons below the age of 45 and to those who have satisfied the requirements for training in neurosurgery as ascribed by the Board of Neurological Surgery, or its equivalent as determined by the membership committee. This is a society primarily designed for the dissemination and promotion of fellowship among young neurosurgeons.

INTERNATIONAL CONGRESS OF PSYCHIATRY

The International Congress of Psychiatry will be held in Paris Oct. 4 to 12, 1950. The scientific program of the six main afternoon sessions is definitely arranged:

WEDNESDAY, OCTOBER 4

General Psychopathology

Subject: Psychopathology of Delusions

Chairman: Prof. F. Morel, Geneva, Switzerland

Speakers: Dr. P. Guiraud, Paris; Dr. Mayer-Gross, Dumfries, Scotland; Prof. E. Morselli, Novara, Italy; Prof. H. C. Rümke, Utrecht, Netherlands

THURSDAY, OCTOBER 5

Clinical Psychiatry

Subject: Application of Testing Methods to Clinical Psychiatry

Chairman: Prof. H. Delgado, Lima, Peru

Speakers: D. Rapaport, Stockbridge, Mass.; Prof. M. Bleuler, Zurich, Switzerland; Dr. A. Guera, Madrid, Spain; Prof. R. Nyssen, Bruxelles, Belgium; Dr. P. Pichot, Paris

FRIDAY, OCTOBER 6

Cerebral Anatomy, Physiology and Biology

Subject: Cerebral Anatomy and Physiology in the Light of Lobotomies and Topectomies

Chairman: Prof. F. L. Golla, Lourdes, France

Speakers: Dr. Alfred Meyer, Lourdes, France; Prof. H. J. de Barahona Fernandes, Lisbon, Portugal; Dr. W. Freeman, Washington, D. C.

MONDAY, OCTOBER 9

Biological Therapy

Subject: Indications for Shock Therapy Methods

Chairman: Prof. J. Handelsman, Warszawa, Poland

Speakers: Prof. J. Lopez-Ibor, Madrid, Spain; Dr. M. Sakel, New York; Prof. U. Cerletti, Rome; Prof. R. Dresser, Poznan, Poland; Dr. L. Meduna, Chicago

TUESDAY, OCTOBER 10

Psychotherapy, Psychoanalysis, Psychosomatic Medicine

Subject: Evolution and Present Trends of Psychoanalysis

Chairman: Dr. Franz Alexander, Chicago

Speakers: Dr. Franz Alexander; Miss Anna Freud, London, England; Dr. R. de Saussure, New York; Dr. M. Levine, Cincinnati

THURSDAY, OCTOBER 12

Social Psychiatry

Subject: Genetics and Eugenics

Chairman: Prof. T. Sjögren, Stockholm, Sweden

Speakers: Dr. F. Kallmann, New York; Dr. J. A. Fraser-Roberts, London; Prof. E. Strömgren, Risskov; Dr. E. Slater, London

The program of the morning sessions, on Thursday (October 5), Friday, Monday, Tuesday and Thursday (October 12), is still to be organized. The topics of the seven sections are as follows: general psychopathology; clinical psychiatry; cerebral anatomy, physiology and biology; biologic therapy; psychotherapy, psychoanalysis and psychosomatic medicine; social psychiatry, and child psychiatry.

An exhibition of psychopathologic art will open in the psychiatric center, Ste. Anne, Paris. Correspondence may be addressed to Dr. Parienté, Hôpital Psychiatrique de Villejuif, Seine.

An exhibition on the history and progress of psychiatry will be given in the Palais de la Decouverte, Paris. Correspondence may be addressed to Dr. P. Deniker, 1 Rue Cabanis, Paris XIV°.

The subscription fee for the members of the Congress is temporarily fixed at 5,000 francs and the fee for the associate members, at 3,000 francs.

Communications may be directed to Dr. Henri EY, general secretary, 1 rue Cabanis, Paris XIV°.